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REGIONAL ILEITIS: A CLINICAL, NOT A PATHOLOGICAL ENTITY*

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FOR the last thirty years there have appeared in medical literature accounts of inflammatory, tumor-like thickenings of the intestinal wall. These have been known to occupy the entire length of the intestinal tract[1] but have usually been confined to some part of the colon. Here they tend, through the obstructive symptoms they evoke, to imitate cancer and doubtless have been mistaken for both cancer and diverticulitis. However, they have also been reported to occur in the small intestine where their effect is rather different. They have generally been given the name, granuloma.

Clinically, the symptomatology of these lesions is rather vague. Erratic sorts of colic usually have been reported; frequent movements of the bowels amounting occasionally to serious diarrheas; the presence of excessive mucus in the movements and occasionally blood; and since the tendency of the thickening is, in the end, to cause obstruction, signs of stoppage have sometimes led to discovery of the mass at the operating table. Some reports have described a rapid course, but, as a rule, the symptoms have been spread out over a long period, indicating a chronic underlying process.

Pathologically, the thickenings are decidedly suggestive of tuberculosis, particularly when they appear in the ileo-cecal region. Yet it has seldom been possible to discover any etiological factor. There is present ulceration, ranging from the mild to the very severe, and a penetrating inflammatory reaction, involving all coats. The effect of this process has been to cause such edema and fibrosis as greatly to thicken the bowel wall and to narrow its lumen. As complications, perforation and fistula formation have occurred, usually to neighboring intestine, but sometimes, after drainage of an abscess or after appendicectomy, to the surface of the abdomen, and the final stage has been closure or near closure of the lumen.

A very good account of what they named "non-specific granulomata of the intestine" was given in 1923 by Moschcowitz and Wilensky[2], who, while failing to discover any characteristic clinical signs or a clean-cut pathological picture, insisted that the thickenings were neither tumors nor specific infections, but that some low-grade sort of bacteria must be presumed to be their cause. They regarded the prognosis as good, pointing out that granulomata are often susceptible of surgical removal and that they may even disappear spontaneously.

More recently, an attempt has been made by Crohn, Ginzburg and Oppenheimer[3] to isolate from the large, non-specific group of granulomata a clean-cut entity which they have named, "regional ileitis." Others have taken up the name, and Clute[4] has reported several cases from the Lahey Clinic. The disorder, as described, and as we have observed it in two instances, has a decidedly chronic character, tending to appear in young adult life, rather insidiously, and somewhat under the guise of a mild ulcerative colitis, in that the patient suffers from frequent movements of the bowels and loses weight. Here the resemblance ends, for ulcerative colitis leads to the appearance of gross or microscopic blood in the movements and to organic changes in the colon, readily detectable by the use of the barium enema. Moreover, redness and ulceration of the rectal wall are usually visible through the proctoscope. Whereas, in ileitis, the large bowel is not affected, the loose movements contain mucus but as a rule no more than chemical signs of blood and the barium enema reveals a normal colon. However, on clinical grounds alone a differential diagnosis of the two diseases can hardly be made. The roentgenologist is indispensable. It is to be supposed that serial roentgenograms after a barium meal will best disclose the abnormal contracted channel through the terminal small intestine. Yet, in both cases here described, a barium enema, flowing back through the ileo-cecal valve, has demonstrated the nature of the disease in the ileum.

As pictured by the group at the Mount Sinai Hospital, the lesion should be situated in the lower ileum just above the ileo-cecal valve, reaching exactly to that point and *not beyond it*. This would imply that inflammatory thick-

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enings elsewhere were of a different character from those found in the terminal ileum and would indicate a process astonishingly specific. Undoubtedly this is the usual location for the lesion in the small bowel but we have seen, in a child, an exactly similar isolated process as part of a dual lesion, at a much higher level Indeed, as has already been stated, earlier reports of intestinal granuloma in the literature suggest a wide distribution through the intestine. However, there is little doubt that the symptom-complex is most characteristic when the disease is confined to the lower ileum, that the disorder is marked here by very decided edema and thickening of the intestinal wall, may complicate the operative procedure. And there is, finally, a tendency to obstruction of the bowel as a result of ever-increasing fibrosis. In our own brief experience we have seen neither of these complications though in our second case a perforation was evidently threatened. Interestingly enough, both the patients observed by us were Hebrews, a fact which suggests a racial influence, especially in view of the considerable group of cases reported from the Mount Sinai Hospital.

A possible relation of the disease to appendicitis, though not proved, is worth mentioning. The appendix in one of our cases was ulcerated and, in the other, was partly destroyed by fibro-

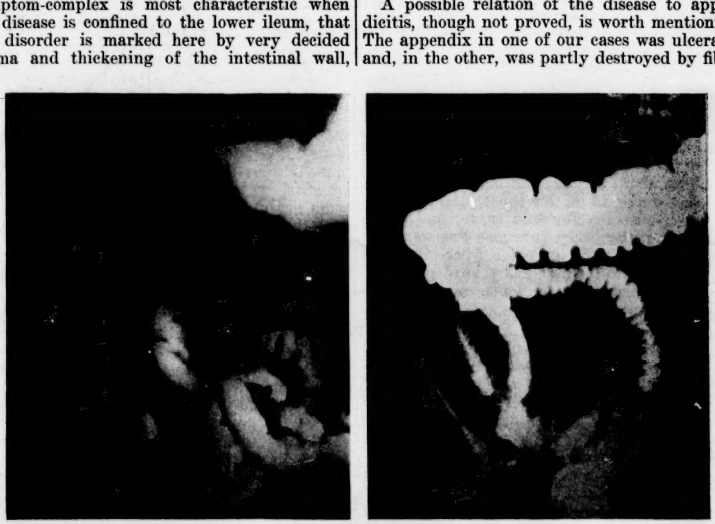

FIGURE 1. Case 1, M. M. G.—Roentgenogram of barium enema which has regurgitated into the small bowel, demonstrating the deformity in the terminal ileum.

Left-hand print. Condition two years before operation. Arrows point to the diseased area on the left. There is a normal coil to the right of it.

Right-hand print. Recurrence of the lesion two years after resection of the terminal ileum and ascending colon. The abnormal bowel is in the same relative situation as in the left-hand print, and in contrast with a long coil of normal ileum beside it.

with an extensive adenitis in the mesentery but perhaps only a very limited amount of ulceration of the mucosa, is associated with mild or severe cramps and diarrhea, with a varying degree of fever, and causes local discomfort and tenderness, more or less accurately localized in the right lower quadrant. It may often be possible to palpate the thickened edematous bowel and mesentery.

As a rule, the character of the malady changes very little over a period of many months or years, yet finally, according to Crohn and his co-workers, the ulcerative, inflammatory process is apt to result in certain complications. There is a tendency to perforation—not such a process as to lead to peritonitis but one which causes a local reaction and the formation of a fistula into neighboring bowel, most often the right colon—a result not evident clinically but which sis. Others have observed that removal of a diseased appendix has been apt to precede discovery of the ileitis. And though it is true that disease of the cecum is unlikely to be associated with ileitis, the vascular relations of the appendix to the lower ileum rather than the cecum undoubtedly favor its involvement in infections of the lowest portion of the small bowel.

PROTOCOLS

Case 1. M. M. G., a man, thirty years of age, a patient of Dr. E. S. Emery, had suffered from diarrhea for about six years. The only significant finding in his previous history was an operation for ischio-rectal abscess, three years before the onset of his present illness. The operation was curative.

The stools were always watery, never contained gross blood and were associated with generalized abdominal cramps. As his illness increased in severity, the number of movements rose to 20-30 a day, attacks of fever, up to 104° F. occurred and

the patient lost over thirty pounds in weight. He experienced several attacks of low abdominal colic which seemed to settle in the right lower quadrant. At one time he was suspected of suffering from an infectious mononucleosis. On this account his tonsils were removed.

About two years before he was seen by one of us, a roentgenological examination of the gastro-intestinal tract showed a fixed cecum and suggested the possibility of tuberculosis. Later a barium enema revealed a normal outline of the cecum but a narrowing and stiffening of the lumen of the lower ileum. This gave the impression of a chronic inflammatory process, probably tuberculosis. The stools, which comprised undigested food and mucus, never contained gross blood. Indeed the guaiac test was sometimes negative though the benzidine was always positive.

Operation, September, 1931, disclosed a remarkable thickening and edema of the lower 40 cm. of ileum. The process began abruptly above, and seemed to end at the ileo-cecal valve. The bowel appeared enlarged to about twice its normal size, its walls being decidedly thickened. Its peritoneal surface was pinkish and smooth. The mesentery of the lower ileum was greatly thickened and loaded with large juicy lymph nodes, numbers of which were felt along the course of the ascending colon up to the level of the duodenum. With a margin of some 20 cm. of healthy-appearing bowel above the lesion, the lower ileum, cecum and ascending colon were removed, and an end-to-side anastomosis, ileum to transverse colon was made. Probably less of the ascending colon would have been resected if it had not seemed desirable to remove most of the mass of lymph nodes which lay mesial to it. As it was, a good many were left in the root of the meso-ileum.

The effect of operation was disappointing. For some days the patient did very well, but soon the diarrhea returned and in a varying degree of severity has persisted during the two years following. Recently it has been discovered that though the colon is quite normal, there is an area in the ileum immediately proximal to it which has exactly the appearance of the original lesion. This would seem to be a recurrence, perhaps a reinfection from the diseased lymph nodes noted above. (Figure 1.)

Case 2 is that of a young married woman, G. B., twenty-six years of age. Soon after the birth of her first baby (which was uneventful) she began to suffer from low abdominal cramps, usually associated with frequent movements, and from colicky pain alternating with dull discomfort in the right lower quadrant. The cramps tended to appear about two hours after her meals. On several occasions she noted, during the two years before she was seen by one of us, several quite severe attacks of the pain in the region of the appendix. There was no fever and there was no blood in the stools, but she was moderately anemic and had lost considerable weight. A vague mass could be palpated in the right lower quadrant.

Roentgenological examination revealed a normal esophagus and stomach, the lower ileum could not be visualized, the cecum was incompletely filled with the barium and there was tenderness mesial to it. Subsequently a barium enema showed a normal colon, but after some delay the enema was regurgitated into the terminal ileum, which appeared small and contracted. (Figure 2.) Proximal to this area the small bowel appeared normal. A tender movable mass was felt in the region of the ileo-cecal valve and suggested tuberculosis.

The blood, except for a slight secondary anemia, was not remarkable.

At *operation*, March 10, 1933, much the same picture presented itself as in the previous case, that is, marked edema and induration, with many enlarged mesenteric lymph nodes, but here there was one particular swollen loop which had become adherent in the pelvis and to part of which the omentum had become strongly attached, suggesting a tendency to perforation. The surface of this loop was covered with tiny tubercle-like nodules. The cecum and appendix appeared normal. About 15 cm. of the ileum was diseased. The impression was given that edema was more noticeable here than in the first case,

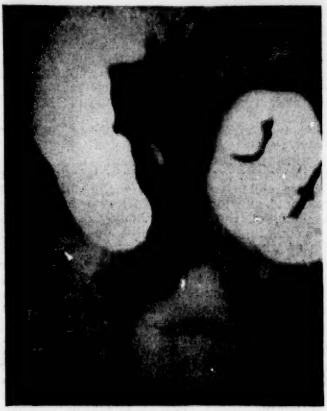

FIGURE 2. Case 2, G. B.—Roentgenogram of barium enema. The greatly contracted channel through the terminal ileum is indicated by arrows, and contrasts well with the coils of normal ileum near by.

and that the condition was probably more acute, as might have been expected from the comparatively brief duration of the disease.

Resection of the lower ileum, cecum and ascending colon was performed with end-to-side anastomosis, ileum to transverse colon.

Recovery was uneventful, but the patient, though in a lesser degree than in the previous case, has continued to suffer from an undue number of loose movements of the bowel, apparently owing to the fact that the remaining colon has not yet acquired the function of the lost cecum and ascending colon. There has been a gain of some thirty pounds in weight.

Pathological Examination

Case 1. (M. M. G.)—The specimen consisted of distal 60 cm. of the ileum, 17 cm. of the cecum and ascending colon, and the appendix. There were several thick, fibrous adhesions between the edematous, indurated folds of the mesentery of the ileum. The mesenteric lymph nodes were slightly enlarged but, on section, there were no visible lesions. At a point 40 cm. proximal to the ileo-cecal valve, there was an abrupt transition from normal intestine to thick-walled ileum (6-8 mm.) that showed numerous mucosal ulcerations between which there were edematous, congested islands of mucosa. The ulcers were irregular in shape, shallow and often confluent. Their bases were flat and their margins undermined. They were diffusely scattered. They ceased abruptly at the ileo-cecal valve. The cecum was slightly contracted but there were no inflammatory lesions of either the cecum or ascending colon. Except for three small mucosal ulcerations, the appendix was negative.

Microscopic Description: Several blocks of tissue were taken from the ileum and regional lymph nodes. Material was fixed in Zenker's Fluid and formalin.

Paraffin sections were stained with eosin-methylene blue for purposes of routine study. The methods of Gram, Giemsa and Goodpasture were utilized for demonstrating bacteria. Numerous sections were stained for acid-fast bacteria.

The salient histological features of the ileum were as follows: acute and chronic mucosal ulcerations, a diffuse, cicatrizing, non-specific type of chronic inflammation which extended from mucosal to serosal surfaces, and hypertrophy of the smooth musculature. The ulcerations of the mucosa were chiefly chronic. A few, which were acute, were covered with a layer of fibrin and polymorphonuclear leucocytes. Usually the lesions were shallow, although occasionally they extended into the submucosa. The intervening remnants of mucosa were edematous, congested and variably altered by a diffuse, active, chronic inflammatory process. Many glands were destroyed. Others were distorted or dilated. In the tunica propria and especially beneath the ulcers there were proliferating fibroblasts and myriads of plasma cells, lymphocytes, eosinophiles and polymorphonuclear leucocytes. Rare multinucleated giant cells of the foreign body type were found. These contained dark granules and irregular fragments of what was presumed to be ingested débris.

The inflammatory cell infiltration extended through the intestinal wall into the serosa and dense cicatricial tissue was prominent in the submucosa and serosa. The widespread fibrosis, together with hypertrophy of the smooth muscle cells and edema, served to double the thickness of the wall. In the serosal fat tissue there were foci of necrosis. Some of these were acute while others had undergone organization. On the peritoneal surface there were small amounts of fibrino-purulent exudate. The regional lymph nodes showed slight hyperplasia of lymphoid cells and an increase in the number of mononuclear cells in the dilated sinusoids. There were no aggregates of monocytes and giant cells as in the other case reported here.

Bacteriological Studies: No organisms, which might be considered as the etiology of this pathological process, were demonstrated in the various special stains of fresh material and paraffin sections. No animals were injected.

Case 2. (G. B.)—The specimen consisted of 25 cm. of the terminal ileum, 20 cm. of the cecum and ascending colon, and the appendix.

An examination of the exterior of the specimen revealed many characteristics, which were most consistent with those of a chronic inflammatory process that had involved the terminal ileum and its mesentery. The proximal 10 cm. of the resected ileum showed dilatation, slight mural thickening and serosal edema. Then, there was a sharp transition to a contracted, thick-walled (5-8 mm.) ileum, which was kinked at an acute angle by firm fibrous adhesions, that bound together the two segments of the distal 15 cm. of the ileum along the line of mesenteric attachment. At the ileo-cecal valve, the thickening of the intestinal wall ceased abruptly. The cecum was constricted toward the ileo-cecal valve. The ascending colon was normal. The appendix, which was retrocecal in position, showed no evidence of an active inflammatory reaction. The mesentery of the ileum was of interest not only because of the edema and induration but also because of its broad attachment to the terminal 15 cm. of the acutely angulated ileum. The mesentery was so thick that the edematous, redundant fat almost encircled the surface of the bowel. Although the peritoneum was injected, there was no exudate. However, the smoothness of its surface was interrupted by scattered, small, elevated, greyish-white, semi-translucent nodules which were restricted principally to the serosa of the ileum. These nodules, which were often confluent, averaged less than 1 mm. in diameter. In many respects they resembled the miliary lesions of tuberculosis.

The intestine was opened in the direction of normal peristalsis and opposite the mesenteric attachment. There was slight thickening of the tunica muscularis of the proximal 10 cm. of the ileum. In this portion the circumference of the lumen was 5 cm. and the mucosa was intact. Beyond it the lumen suddenly became small (2.5 cm. in circumference) and the bowel wall very firm and thick (7-10 mm.). The increase in thickness was due principally to edema, fibrosis and muscular hypertrophy. (Figure 3.) These pathological changes were accompanied by deep, irregular, confluent, mucosal ulcerations which were continuous to the ileo-cecal valve and were limited chiefly to the mucosa that was closest to the attachment of the mesentery. They were most extensive at the apex of the sharp angulation of the ileum, formed a longitudinal gutter bounded by edematous folds of mucosa, and diminished in size and number toward the ileo-cecal valve. The narrow, rigid, distorted, ileo-cecal valve was lined with edematous mucosa, which was furrowed with ulcerations that extended only for a few millimeters into the cecum. This minor involvement and the consequent cicatrization had served to deform the regional cecum but the major portion of its structure, as well as that of the ascending colon, was normal.

The appendix was covered by smooth serosa to which a few fibrous adhesions were attached. Only the proximal 10 cm. of the lumen were patent, the remainder having been obliterated by cicatricial tissue. The mucosa of the proximal part, although atrophic, was not ulcerated.

Several enlarged mesenteric lymph nodes, which varied from 10 to 15 mm. in length, were found in the region of the ileo-cecal valve. On section, the lymphoid tissue was soft, greyish-pink and hyperplastic. Irregular, translucent, elevated areas suggested the possibility of miliary tubercles in the lymphoid tissue but there was no caseation, necrosis or calcification.

Microscopic Description: Several blocks of tissue from the ileum, mesentery, lymph nodes, cecum, colon and appendix were fixed in Zenker's fluid, Regaud's fluid, absolute alcohol and formalin. Paraffin sections were stained with eosin-methylene blue as well as hematoxylin and eosin. The methods of Gram, Giemsa, Verhoeff, Goodpasture and Levaditi were utilized in an attempt to demonstrate bacteria. Numerous sections were stained for acid-fast organisms.

Despite the fact that the mucosa in many areas was destroyed by the chronic inflammatory process, the wall of the ileum was two or three times its normal thickness. This was due chiefly to hypertrophy of the musculature, edema and an increase in the amount of connective tissue. The few islands of mucosa, which remained between the extensive, confluent ulcerations, were edematous, engorged and infiltrated with numerous lymphocytes, plasma cells, polymorphonuclear leucocytes and eosinophiles. Most of the ulcers showed slightly undermined edges and flat bases, but a few cleft-like ulcerations penetrated deeply into the submucosa. The bases of the ulcers were covered with an exudate of fibrin and polymorphonuclear leucocytes, beneath which there were a well-vascularized chronic granulation tissue and dense cicatricial tissue, infiltrated with numerous lymphocytes and plasma cells, scattered eosinophiles and few polymorphonuclear leucocytes. Cells of the lymphoid series were predominant in all areas and many germinal follicles were found. In the chronic granulation tissue there were a few multinucleated foreign body giant cells. These contained particles of débris and, not infrequently, there were narrow clefts which were presumably evidence that some of the ingested material had been

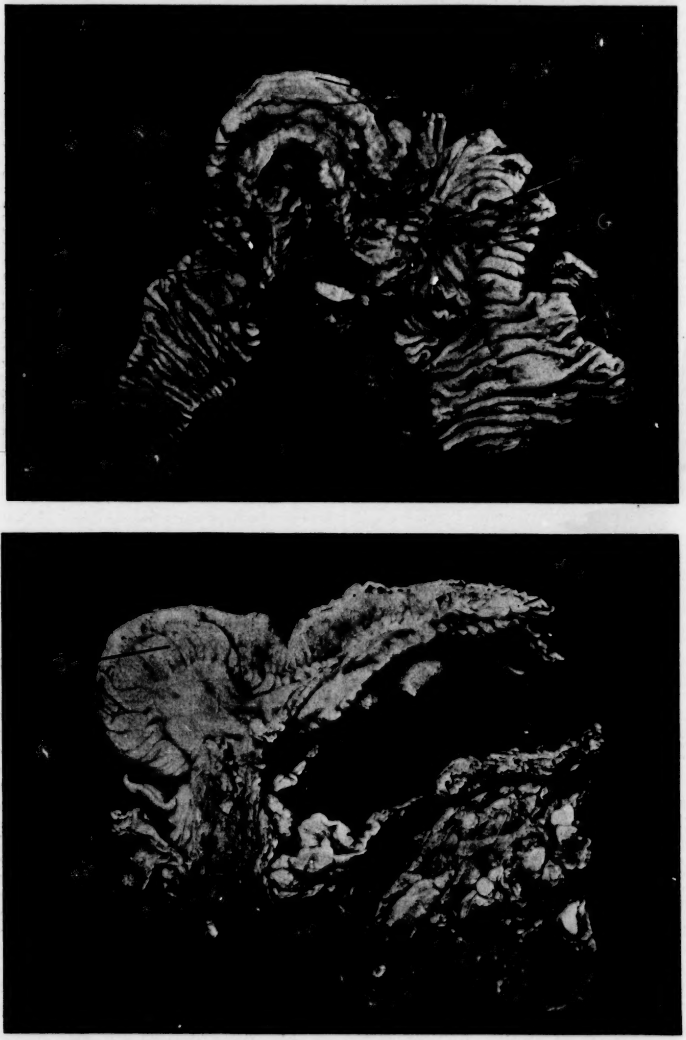

FIGURE 3. Case 2, G. B.—Photograph of the distal ileum, cecum and ascending colon.

Upper figure. The intestine has been opened opposite the mesenteric attachment. (A), Normal ileum. (B), The beginning of the mucosal ulcerations. (C), Adhesions which bound together the two limbs of the loop of ileum. (D), The gutter-like ulcerations adjacent to the attachment of the mesentery. (E), The thick wall of the diseased ileum. (F), The ileo-cecal valve, beyond which there were no ulcerations. (G), The contraction and slight deformity of the cecum due to cicatrization at the ileo-cecal valve.

Lower figure. The reverse side of the specimen. (A), Normal mesentery of the normal part of the ileum. (B), The edematous, thick mesentery of the diseased portion of the ileum (C), Normal mesentery of the cecum.

dissolved by solutions used in preparation of the tissues.

The most puzzling features of the histology were the cellular aggregates, which closely resembled the miliary lesions of tuberculosis. These lesions were scattered throughout the deep portions of the granulation tissue and in the submucosa. They were very rare in the tunica muscularis and serosa. Several were found in the mesenteric lymph nodes. The earliest evidence of tubercle formation was an accumulation of large endothelial leucocytes. In the larger lesions, these large mononuclear cells were fusiform, globular and multiangulate. The cytoplasm was vacuolate and, not infrequently, the cells had fused to form multinucleate giant cells. There were no typical epithelioid cells, areas of caseation necrosis or deposits of calcium. Vestiges of former lesions were composed of connective tissue cells, collagen, and remnants of mononuclear cells.

The chronic inflammatory reaction in the mucosa and submucosa was continued along the connective

FIGURE 4. Case 2, G. B.—Microphotograph of a section of the diseased intestinal wall, about × 100, showing a large foreign-body giant cell (above) and several tubercle-like lesions (below it) in the midst of a chronic inflammatory reaction in the mucosa. An exactly similar appearance is found in the lymph nodes.

tissue septa through the tunica muscularis into the serosa. In the submucosa, fibrosis was prominent. In the serosa, a great increase in the connective tissue, engorgement of vessels, dilatation of lymphatic channels and accumulations of lymphocytes were the salient findings. The aggregates of lymphoid cells were responsible for the small tubercle-like lesions noted in the gross examination of the serosa of the ileum. Although there was some fibrosis of the tunica muscularis, the great increase in the thickness of this layer was due principally to hypertrophy of smooth muscle cells and edema. Edema was also prominent in the mesentery, while dilatation of lymphatic channels, engorgement of blood vessels, fibrosis and infiltrating lymphoid cells were found in those areas where the inflammation was most severe. Near such areas there were regional lymph nodes characterized by fibrosis of capsules, hyperplasia of lymphoid cells, accumulations of large monocytes in the dilated sinuses and scattered tubercle-like lesions of the type described above. (Figure 4.)

The sections of the cecum, colon and appendix were of little interest. Except for hyperplasia of lymphoid cells in the solitary follicles, the cecum and colon were negative. The mucosa of the appendix was atrophic and almost entirely replaced by dense cicatricial tissue. There were no ulcerations or aggregates of mononuclear and giant cells, such as were found in the sections of the ileum and mesenteric lymph nodes.

Stains of the tissues by the methods of Gram, Giemsa, Verhoeff, Levaditi and Goodpasture disclosed no organisms which might be considered a cause of the disease. The stains for acid-fast bacteria also were negative.

Bacteriology: Tissue from lymph nodes and the serosa of the ileum was macerated. Some was planted on artificial culture media. The remainder was injected into animals. Deep tubes as well as slants of the following media were incubated under aerobic and partially anaerobic conditions at 37.5° C.: dextrose blood agar, chocolate blood agar, hydrocele agar, egg-yolk agar, dextrose brain broth, and Sabouraud's medium. All cultures showed no growth. Material was injected into two guinea-pigs and one rabbit. The injections into the guinea-pigs were intratesticular, intraperitoneal and subcutaneous. The rabbit was injected subcutaneously, intraperitoneally and intracerebrally. The animals remained healthy and were sacrificed ten weeks after injection. No pathological lesions were disclosed by either the gross or microscopic examination of the tissues.

DISCUSSION

The two specimens here described are examples of a pathological process designated by the authors to whom we have already referred as "regional ileitis" and held by them to be a clinical and pathological entity. We agree that a terminal ileitis presents a rather characteristic clinical picture but acceptance of the local lesion as a pathological entity is certainly premature since criteria are lacking by which one can segregate this granulomatous process from similar lesions occurring elsewhere in the intestinal tract. Moreover, it is by no means certain that the disease in both our cases is of a similar nature and due to an identical etiologic agent. In both instances the pathological process was characterized by a chronic, proliferative, inflammatory reaction in which the most outstanding features were extensive mucosal ulcerations, thickening of the wall and constriction of the lumen of the ileum. The cecum, except for slight deformity, and colon were normal. Thick adhesions between folds of edematous mesentery and enlarged mesenteric lymph nodes completed the important gross anatomical similarities. The specimens, microscopically, were similar in that the general appearance of the chronic inflammation of the ileum, the mesentery and lymph nodes in most respects was the same, even to such detail as scattered foreign body giant cells in the ileum.

However, the two specimens differed in three respects. First, there was a difference in the position of the mucosal ulcerations. In one case they were uniformly distributed and in the other they were restricted almost entirely to the mucosa adjacent to the attachment of the mesentery. Secondly, in one case there were numer-

ous, focal, miliary, tubercle-like lesions in the ileum and lymph nodes, but in the other, these lesions were lacking in all sections. They more closely resembled the tubercles of so-called Boeck's sarcoid than those of tuberculosis, which we believe to have been excluded here. For this reason certain observers have designated the disease as "sarcoid of the intestine." It is our opinion that the giant cell reaction and the formation of tubercles is a response to a foreign body, which, in all probability, in the majority of instances is a lipoid. In various reported cases, the descriptions of vacuoles, clefts, and refractile, "crystalline," shred-like structures within and adjacent to the giant cells are consistent with this interpretation. Dr. Henry Pinkerton[5] (Private Communication), who has made careful studies on the reactions to various oils and fats in animal and human lungs, has been good enough to express his opinion of the giant cell and tubercle formation in the ileum and lymph nodes of the cases herein reported. He states that this reaction is very similar to that which can be reproduced experimentally by injections of animal oils and is unquestionably a response to a lipoid substance. Whether this lipoid gains access to the tissues from the lumen of the bowel or whether obstruction of lacteals is a factor are questions that can only be answered after more complete study. Thirdly, there was a scarred appendix in one specimen and there were active, chronic ulcerations of the appendiceal mucosa in the other. Only in this particular, did our material differ from that of Crohn, Ginzburg and Oppenheimer. They state that "the appendix is always free from guilt and free from changes." This alone is not sufficient reason for our hesitancy in accepting "regional ileitis" as a pathological entity. They state that "we now know that the process never transcends the limit of Bauhin's valve." Certainly this is not in keeping with Case 1 reported by Moschcowitz and Wilensky, in which the ascending colon as well as the terminal ileum was involved. Finally, we refer, by the kind permission of Dr. W. E. Ladd, to a patient under his care at the Children's Hospital, Boston. This child had two diseased loops of small intestine: one in the jejunum and the other in the distal ileum. The gross and microscopic anatomy of each loop was identical with that of Case 2, herein reported.

Therefore, it is our belief that "regional ileitis," defined as a pathological entity which affects only the terminal ileum and which never extends beyond the ileo-cecal valve, is not acceptable as such. Rather, it is a granulomatous process of unknown etiology which should be carefully sought for at any point along the entire length of the intestinal tract.

Clinically, the symptom-complex due to an inflammatory ileal thickening, as already described, is fairly definite. Yet it is by no means certain that every ileitis runs a chronic course. There may be less persistent forms which disappear spontaneously. Recently Rockey[6] has published an account of four cases in children which presented a picture of acute appendicitis. In each instance, operation disclosed a thickened inflamed ileum, masses of enlarged lymph nodes in its mesentery and a normal appendix. At each operation Rockey, having opened the abdomen, removed the appendix but felt that he could do nothing for the ileitis. Yet all the children recovered, the local symptoms subsiding in a few days to two weeks. It is a pity that the subsequent story of these patients is not known. On the face of the report, however, the disease subsided without trace and without treatment. One might predict that spontaneous cures are possible from accounts of the disappearance of ileal thickenings following side-tracking operations. It would seem that even a well-established change of this sort is reversible.

Finally, in regard to treatment, it has seemed obvious to most operators that the thickened intestine should, if possible, be excised. Yet in our two cases the results of such radical treatment were not entirely successful. Both patients are improved, the second decidedly so. But the first has suffered a recurrence and is about to be subjected to a second operation. May it not then be true that the attempt to excise a supposedly infectious lesion is unwise? In other parts of the body one would expect the infection to persist and even to be spread in a dangerous manner. Would it not be better, therefore, to begin with a side-tracking operation, joining the ileum, proximal to the lesion, to the ascending colon? Should this operation prove curative, no more will be required. Should it fail, or incompletely relieve the patient, the diseased bowel, at a second stage, can be removed. Such a procedure is planned for the patient already subjected to a very radical removal who is now suffering from a recurrence of the disease.

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DISCUSSION

DR. HOWARD M. CLUTE, Boston, Mass.: The interest which we have had in regional ileitis started with the paper by Crohn, Ginzburg, and Oppenheimer, in 1932, in which they discussed as a clinical entity, this inflammatory process involving the terminal ileum.

From their studies, which Dr. Homans has discussed, they felt that it was due to a non-specific inflammation involving the mesentery and the wall of the last foot, or eighteen inches of the ileum.

The clinical symptoms that arise in this disease, which I believe make it somewhat a clinical entity, will naturally vary, it seems to me, with the type of infection and with the activity of the infection and the duration of the infection in the wall of the ileum.

Since the summer of 1932, we have had four cases that we feel can definitely be called regional ileitis. We had previously reported two, as Dr. Homans said and since then have fortunately seen two more, and it seems to me that these four cases had the varying clinical symptomatology which may arise in the disease as the activity of the disease varies.

The first patient, previously reported, had his appendix removed some twelve years before. He came into the hospital because of duodenal ulcer and was doing well on medical management when he developed a vague, distressing pain in the right lower quadrant which soon became more pronounced. Finally he had a temperature of 99½°, his white count was elevated, and he had all the clinical signs of inflammatory appendicitis. We decided to operate on him, for we thought it might be a regional ileitis since his appendix had been removed. Other than that we had no proof of ileitis being present.

At operation we found a marked inflammatory process, involving the mesentery and wall of the ileum: edema, and hypertrophy of the lymph nodes and thickening of the wall of the ileum. In the mesentery was an abscess which contained a half ounce or more of pus. We drained the abscess and did nothing about the inflammatory reaction in the ileum.

He made a very good recovery and within a week I have seen him. He is now having some vague pains and disturbances in his abdomen. Dr. Kiefer felt that probably those could well be due to the old duodenal ulcer, but I feared they might be due to the inflammatory process; however, they are not so serious that he is in any way incapacitated. This case I interpret as being an acute inflammatory reaction in the mesentery and the wall of the ileum of relatively short duration.

The next two cases illustrate the cases which Dr. Homans has discussed in which the process is less acute and of much longer standing. The first of these men had been having symptoms for several years, and serious symptoms some two years before his operation.

He was seen to have, by x-ray, some obstructing lesion in the terminal ileum and at operation Dr. Lahey found a very marked hyperplastic process involving the wall of the terminal ileum for a distance of a foot or more from the cecum. He thought it was probably tuberculous. He did an ileocolostomy with the idea that when the man's condition improved, he would do a resection. In some six weeks, however, the man gained twenty pounds in weight and examination showed no mass. His general condition was so satisfactory that we decided to wait. Ten months have passed and he is still in excellent condition and health, and has no symptoms. We consider that he doubtless had regional ileitis.

The second case in the chronic inflammatory group was another man who had had symptoms for two years with great loss of weight, attacks of colic and distention, who was only diagnosed as ileitis by thinking that possibly he might have some such lesion. On taking serial plates, after a bismuth meal it was shown that there was delay in the ileum. At operation he showed hyperplastic thickening of the terminal ileum, which was adherent to the sigmoid. In freeing it from the sigmoid, the ileum was perforated and could not, therefore, be readily repaired; therefore, a resection of the terminal ileum was done with an end-to-end anastomosis and also a lateral anastomosis to make sure no obstruction occurred. That was eight or nine months ago. He is doing pretty well, but having some symptoms of pain and distress.

If the inflammatory process of regional ileitis goes on still further, with acute exacerbations, we should expect a different pathology, though it is all due to the simple, fundamental, inflammatory process.

We had one patient, a woman of sixty-nine, who some years before had had an abdominal operation with two later operations for intestinal obstruction. She had a large mass in the right lower quadrant with obstructive symptoms. She was extremely thin and very ill. After considerable hesitation, we operated and resected the last three or four feet of ileum which was bound together with multiple fistulous openings running through in every which-way from one loop of gut to another.

Dr. Shields Warren was unable to say what the pathology was other than a chronic inflammatory process invading the wall and giving multiple fistulous communication; therefore, we consider her to be a type of regional ileitis. It is over a year since we operated and she has no further symptoms. She is quite well and better than she has been for some little time before this.

I agree perfectly with Dr. Homans that regional ileitis is not a pathological entity except as inflammation in a specific organ gives specific pathology in that organ. I feel, however, that it is a most interesting clinical entity and I believe that we may be able to make the diagnosis only because of the recent interest which has come by observing this condition as a clinical entity.

DR. WILLIAM E. LADD, Boston, Mass.: I think this subject has been somewhat confused and is still somewhat confused in spite of Dr. Homans's most interesting paper. The reasons for this confusion are that we don't know the etiology and that a great variety of symptoms and pathological findings have occurred. The same condition has been given different names and different conditions the same name.

We have had two of these cases at the Children's Hospital. The first one was a child, seven years and three months when he came to our service, and the illness had dated from the time he was nine months old. Up to the age of nine months he had gone along with the perfectly normal development of an infant and arrived at the weight of 21 pounds, and had had no symptoms.

At the age of nine months he began having vomiting, had considerable loss of appetite, and at eighteen months weighed two pounds less than he did at nine. He was then followed with very careful medical supervision for a matter of three and one-half years. He had a very good family pediatrician who had frequent consultations with other men, and he was very carefully supervised and carefully investigated to try to find out what was the cause of his illness.

During the next three years he had symptoms of vomiting, pain, refusing to eat, but in spite of that, gained up to thirty-five pounds in weight. Following that, with still continued care, he went downhill, so that at the age of seven years and three months he weighed twelve to fifteen pounds less than he did at the age of three and one-half.

At that time he was reported by the nurse who

was taking care of him, to have at times visible peristalsis. As I saw him, I could see no intestinal patterning and no visible peristalsis, and all he presented was a very small, poorly developed child, with dry skin, a fussy manner, and unwilling to eat. He had from time to time more severe symptoms of real colic, pain, and vomiting.

In March, 1932, an exploratory operation was decided on and I opened the abdomen, examined the contents, and found in the lower jejunum perhaps two to three feet of very much thickened intestine, with the fat from the mesentery extending up over its walls just as in the second specimen that Dr. Homans showed, and the serosa studded with tubercles which I think Dr. Homans describes very well, saying that they are reminiscent of, though not exactly like, tuberculosis. However, we considered the possibility of tuberculosis. I didn't do a resection at that time. I did a biopsy from the glands of the mesentery and took out one or two of the small tubercles for pathological examination.

Following that the symptoms became worse and six weeks later he was developing perfectly definite signs of obstruction. I forgot to state that in the first exploratory we also felt in the terminal ileum about a foot of intestine in which was apparently just the same process, only it had advanced less far, was less thick and apparently its lumen was less narrow.

Six weeks after the first operation we did a resection of thirty inches of the lower jejunum and upper ileum and a lateral anastomosis. Following this procedure the child did extremely well, gained in a very short time five or six pounds in weight, took his feeding better than he ever had in his life, and was progressing very well. That was in April, and some time in June, about two months later, his symptoms returned, but this time were localized in the right lower quadrant where we had felt the other mass, and not in the epigastrium as before, so we again did a laparotomy and found that the condition in the terminal ileum had progressed very considerably.

The lumen of the ileum was very much narrowed, and here we did a resection of ten or twelve inches of the terminal ileum and a lateral anastomosis between the ileum and the ascending colon.

Since that time the child has not been a brilliant success, but he has been better than he was before. He has gained back to his maximum weight, but he has from time to time some pain, a dislike of food, and some diarrhea.

I don't know what the end result is going to be. I heard from him last week and he had been very well this summer except for one rather bad setback following a cold.

The other case that we have is one that Dr. Mahoney operated on last June, which I suppose we might include under the general term of ileitis, but it seems to me it is really quite different from the first case. This patient was seven years old, a child who, I take it from his name, was Irish and not Hebrew, like the first one, and had symptoms of acute obstruction rather than a long, prolonged illness.

He had had his appendix removed two or three years prior to this attack, so that that did not confuse the diagnosis and the signs were those of vomiting, pain, tenderness in the right lower quadrant, and abdominal distention.

At operation in this case the terminal ileum was found very much thickened. It was not studded with tubercles, but there was a certain amount of thickening of the wall of the ileum. The process apparently involved all layers. Resection was done in this case and lateral anastomosis performed but this child, contrary to the other, has gone along with a perfectly normal convalescence and has remained perfectly well.

I feel that probably these two conditions should not be included in the same group. There is enough difference in them to make two classifications; however, I think until we discover the etiology of these conditions, this is difficult to do. The chronic type might be grouped under one of the names sarcoid, granuloma or chronic ileitis, while the acute type might be classified as acute ileitis. To group them all under the name of regional ileitis seems to me confusing rather than simplifying.

Dr. Wolbach says, in regard to the etiology of our second case, that it is difficult to believe that this process began as a mucosal infection. The lesions in the small blood vessels suggest that they began at this site, and possible volvulus or intussusception took place with damage to the vessels, and suggests thrombosis. As evidence of an infection, large lymphoid follicles, and marked inflammatory cell infiltration were present.

I think that this case is similar to the other ileitis cases that are described as being of an acute nature, but it offers a very much better prognosis than the first case.

DR. C. G. MIXTER, Boston, Mass.: I have been very much interested in this presentation because it so happens that in the last three years since I have been associated with the Beth Israel Hospital, I have had an opportunity to see several of these cases. Whether it has to do with a predilection for the race, I don't know, but there are eight cases that we have classified as regional ileitis. The diagnosis of three of these may be somewhat in doubt because they were not subjected to pathological study. Five cases have been resected. The last resection I did this morning and the pathology is not available.

The other four cases are similar to those that Dr. Homans spoke of and characterized by a chronic inflammatory process limited to the terminal ileum with ulceration, and the ulceration as it diminishes toward the oral limit of the disease is characteristically on the mesenteric margin of the intestine. It may in that way be associated with the mesenteric circulation, but certainly that is the spot at which the marked ulceration occurs.

In regard to the statistics of the cases operated on, of the four resected cases that have been running for some time, three have done well. Two I have seen within the last few days and they are in perfect health. One case still shows a small fistulous opening and diarrhea, but he has put on twelve to fifteen pounds in weight and has been definitely improved.

There is a marked tendency toward fistulous formation in these cases and the case I did this morning in an elderly man, who came in with an abscess in the right iliac fossa unassociated with his appendix, which was at that operation inspected by the surgeon, found to be normal, and not removed. He had obstruction. The abscess was drained. He had an ileostomy, and in removing the ileostomy tube some weeks later, obstructive symptoms supervened and now about six weeks after the primary operation, I did an exteriorzation operation of the Mikulicz type.

I wish particularly to speak about the cultural findings because those, I think, are interesting, particularly in one case. We have searched these cases for any possible organism, such as by maceration and injection and one thing or another; we have ruled out tuberculosis, and there has been no evidence of actinomycosis. One specimen was carefully handled and the ulcers were washed and cul-

tures taken, and one of the enlarged mesenteric glands was cultured, and a moderate excess of straw-colored fluid was also cultured. All three cultures showed a slow-growing type of streptococcus. Other than that, we haven't found anything bacteriologically, but it was interesting that in this particular case I am speaking of, although the straw-colored fluid looked like the usual transudate and the accompaniment of his obstructive symptoms, yet we were able to culture streptococcus from it.

DR. EDWARD H. RISLEY, Waterville, Me.: I should like to ask if negative Wassermanns were obtained in all these cases. That was not mentioned.

DR. JOHN HOMANS: As for the Wassermann reaction, in both my patients I am quite sure the Wassermann was negative and this condition, so far as the pathology is concerned, is in no way suggestive of syphilis. As for conservatism in treatment, I wish to make myself a little more clear. It seems to me that in any other part of the body, if we were dealing with a recognizable infection, or even anything that appeared to be an infection, we would not try to cut it out. If we did, we would expect to spread the disease. Here we are dealing with what looks like an infection and yet we attempt to excise it. This does not seem right.

The reports of the New York investigators are to the effect that "the patient is well after operation." I dare say we would get better results than I think I have obtained, if we used the rather graded surgery which seems safer and more likely to be effective than the immediate resection.

AN EVALUATION OF SIGNS AND SYMPTOMS IN THE DIAGNOSIS OF EXTRA-UTERINE PREGNANCY*

Review of 90 Cases

BY A. F. JONAS, JR., M.D.†

A TYPICAL case of extra-uterine pregnancy is unmistakable; yet an atypical case, even after rupture, may deceive the most astute clinician. Because of the deceiving features of these atypical cases, I have reviewed a series of cases in order to evaluate the various signs and symptoms of the condition. The material reviewed comprises 90 consecutive cases occurring in the Peter Bent Brigham Hospital during the years 1913-1932 inclusive. There were 88 patients, 90 cases in all, since two patients each had recurrence in the remaining tube and consequently presented distinct diagnostic problems on each occasion.

INCIDENCE AND PAST HISTORY

As shown in figure 1 the patients ranged in age from 17 to 41 years, over 96 per cent of them being from 21 to 40 years inclusive. The

FIG. 1.

majority had borne few children, most of them having been primiparae or para one or two before the ectopic gestation. Figure 2 clearly bears out Behney's statement[1], "Parity is no guarantee against future ectopic pregnancy, but the probability of its occurrence is in inverse proportion to the number of intra-uterine pregnancies." Thirty-two cases or 35 per cent had had one or more miscarriages or stillbirths. The relationship between previous abdominal opera-

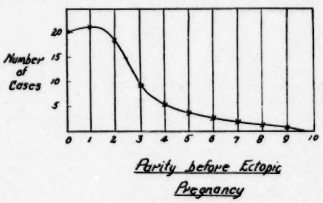

FIG. 2.

tions and extra-uterine pregnancies is prominently cited in the literature, yet only 23 cases or 25.5 per cent had had previous low abdominal or pelvic operations (chiefly appendicectomy and uterine suspension). An additional 14 cases had had dilatation and curettage. Of the 37 cases having had previous abdominal operations or dilatation and curettage, 22 or 59.2 per cent had had no further pregnancy until the ectopic one. Gonorrhea is said to be the chief etiologic factor in extra-uterine pregnancy but only 17 patients gave a history of gonorrhea or showed findings consistent with it at operation.

It is important to appreciate the fact that the patients entered the general surgical wards merely as ill women and not as pregnant ones, and the pregnancy, if the patient was aware of it, seemed a secondary consideration. Twenty-eight women were certain that they were not pregnant, they were unmarried, they had used contraceptive measures, they had not borne children for years, and many more than this

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number had noticed none of the early symptoms of pregnancy, no morning sickness, no skipped periods, no breast changes. Concomitant signs of pregnancy were infrequent.

LOCATION OF PREGNANCY

Forty-eight of the ectopic pregnancies occurred in the right Fallopian tube, and 36 in the left, a ratio of four to three which appears of no significance since the distribution is reported as equal in the larger series of other investigators. In one patient who left the hospital against advice after the diagnosis had been made, and in whom rupture occurred one week later, the location is unknown. Pregnancy occurred in the right ovary in two cases giving a clinical picture identical with the tubal variety. An old lithopedion of 10.5 cm. representing a pregnancy of about three and one half months was found in the left tube of one patient. While pregnant five years before she had been struck by an automobile, suffered abdominal cramps for a month, and thereafter resumed her normal menstrual cycle. She entered the hospital because of severe constipation intermittent with attacks of diarrhea. The only physical finding was a mass involving the left adnexae felt per vaginam. The diagnosis of lithopedion was made by x-ray. Another patient entered the medical service because of diarrhea which was quickly checked. An entirely asymptomatic pelvic mass was discovered and diagnosed as ovarian cyst. At operation two pregnancies were found, one an old calcified fetus in the right ovary, and a smaller, more recent pregnancy attached solely to the omentum. Most interesting is the one case of uncomplicated abdominal pregnancy. This patient had been flowing profusely and almost steadily for two months prior to admission. For one month she had experienced intermittent cramp-like low abdominal pains. The uterus was found to be twice its normal size; an indefinite mass of questionable tenderness was felt in the left lower quadrant. The suspicion of extra-uterine pregnancy was strong enough to demand laparotomy which revealed a perfectly formed 9 cm. embryo with placental attachment to the small intestine and tabs of sigmoid. Recapitulation of the various locations shows:

Tubal pregnancy	
right	48
left	36
Right ovarian pregnancy	2
Right ovarian lithopedion with omental pregnancy	1
Left tubal lithopedion	1
Uncomplicated abdominal pregnancy	1
Site unknown	1
	90

PAIN

All but two cases manifested some kind of pain; that is, pain was a feature, and a prominent one in 97.7 per cent of the cases. In the typical case a very severe pain of sudden onset was preceded by hours to weeks of irregular lower abdominal colicky pains or perhaps by only a mild sense of distress and discomfort. These premonitory pains recurred at intervals, might be absent for days to weeks before the onset of severe pain, and were themselves often disregarded by the patient. Careful questioning of an intelligent patient usually elicited the distinction that the pain commenced suddenly at one point such as the left iliac region or just beneath the symphysis, and then spread rapidly to embrace a wider area such as the whole lower abdomen, the latter localization being the only one obtainable from the less intelligent patient.

Thus the point of initial pain is of considerable diagnostic value if it can be accurately ascertained. This is exemplified by the case of one patient who entered the hospital complaining of right upper quadrant pain with tenderness in the right hypochondrium. Prostration and signs of acute blood loss were so pressing that operation was performed on the diagnosis "Ruptured Viscus, probably Gall Bladder." Following the removal of a ruptured right tubal pregnancy the referring physician's story was obtained. He had seen the patient within two hours of onset and at that time her complaint had been severe right iliac pain with tenderness.

In the Brigham Hospital records the severe pain is variously described as sharp and knife-like, crampy and colicky, or bearing-down like the pain of labor. It frequently caused the sufferer to double up, made movement almost impossible during its height, and lost its greatest intensity within half an hour, continuing less severely for a day or so thereafter, leaving a sense of residual soreness. In this series pain discretely localized to one side or the other of the lower abdomen invariably indicated the side of ectopic gestation, but generalized abdominal pain with only slight preference for one side proved a fallacious localizing symptom. Radiation of the pain was infrequent, but in six cases it darted sharply down the anterior aspect of the thigh on the side affected. In four instances the pain was referred to one shoulder, not always that corresponding to the affected tube. Following rupture, urinary symptoms, usually frequency and burning micturition were observed in 20 cases, and pain on defecation in 13 cases. These special types of pain when present are valuable in confirmation of the diagnosis.

MENSTRUAL HISTORY

The textbook picture of extra-uterine pregnancy requires amenorrhea as a feature, yet only 54 patients or 60 per cent had missed one or more periods. Eighty-one or 90 per cent of the cases showed bleeding per vaginam at one time or another. There was no characteristic type of flowing, no one type being seen in more

than a few of the cases. The blood was usually fresh, occasionally there were gushes of bright red blood, occasionally the passage of clots, and infrequently a foul brownish discharge. In general it so resembled the normal menstrual flow that the patient often confused the abnormal bleeding with her menstrual period and believed it merely prolonged. A number of cases showed intermittent flowing from two to eight weeks in duration, others alternated spotting and flowing with short periods of amenorrhea, others spotted transiently, and in several of the acute cases, a gush of bright blood simultaneous with severe pain was the only bleeding manifested externally. Irregular flowing continued for a number of weeks after rupture in a few of the cases.

VOMITING AND FAINTING

Vomiting, distinct from that of morning sickness, occurred in 20 cases or 22.2 per cent. It was not a prominent symptom, most of the patients returning undigested food, and doing so only two or three times. Its inconstancy and mildness serve as differential points from intestinal obstruction and acute appendicitis. Fainting was seen in only 12 cases, mainly those of acute blood loss.

ABDOMINAL EXAMINATION

Seventy-eight cases or 86.6 per cent showed tenderness, mostly localized to one of the hypogastric regions. Often the tenderness was general throughout the abdomen or lower quadrants with a smaller area of maximal tenderness. Discrete point tenderness was rare and in only five cases was there generalized abdominal tenderness without any localization. Abdominal tenderness is a fallacious guide, however, for in several instances it was observed in the upper quadrants, and in 12 cases, mainly old, it was entirely lacking. Moreover, in two acute cases it was absent. Tenderness in a costovertebral angle was noted twice, and in two cases, abdominal palpation elicited pain in one of the scapular regions. Thus tenderness is by far the most important abdominal sign, spasm ranking next in importance with 25 cases or 27.7 per cent. A palpable mass other than uterus was found in 19 cases or 21.1 per cent, and distention was observed in 12 cases or 13.3 per cent. Shifting dullness was noted 11 times. Minor signs such as rebound four times, and psoas sign once, were noted, but not a single case exhibited Cullen's sign or bluing of the umbilicus.

FREQUENCY OF SIGNS AND SYMPTOMS

	Total	28 Acute	32 Recent	27 Old	3 Unruptured
Pain	88	28	32	25	3
Bleeding	81	21	30	27	3
Abdominal Tenderness	78	26	29	20	3
Vaginal Tenderness	73	25	29	16	3
Vaginal Mass	54	9	23	22	0
Softening of the Cervix	26	9	8	7	2
Abdominal Spasm	25	11	10	3	1
Vomiting	20	—	—	—	0
Urinary Symptoms	20	4	7	9	0
Abdominal Mass	19	2	6	10	1
Cervix Painful to Move	18	6	8	3	1
Pain on Defecation	13	2	7	4	0
Fainting	12	—	—	—	0
Distention	12	4	6	2	0
Shifting Dullness	11	9	2	0	0
Rebound	4	4	0	0	0
Costovertebral Tenderness	2	2	0	0	0
Psoas Sign	1	1	0	0	0

PELVIC EXAMINATION

Vaginal examination revealed a mass in the vaults or posterior culdesac in 54 cases or 60 per cent while a questionable mass interpreted as "fullness" was noted in an additional five cases. Under ether examination, an even larger number of masses were felt. Character of the mass is slight aid in differential diagnosis; the masses as described varied from the size of a hazelnut to that of a large grapefruit; generally they were soft and boggy without fluctuation, and in only a few of the older cases with pelvic hematocele were hard or resistant. The cervix was soft in only 26 cases or 27.7 per cent, and movement of the cervix was painful in 18 cases, or 20 per cent, a reliable sign when present.

Seventy-three or 81.1 per cent showed tenderness on vaginal examination; 17 or 18.9 per cent were not tender, and although these were almost all old cases, three cases of acute rupture lacked tenderness entirely. In most cases tenderness was limited or at least maximal at one point such as the posterior culdesac or one of the vaults, and in only a small group, 18.9 per cent, was it so generalized throughout the vagina that no localization was possible. The rectal findings proved of little value in diagnosis; less could be made out than on vaginal, and their value seems largely confirmatory.

TYPES OF CASES

By dating from the time of operation backward to the onset of severe pain or signs of collapse, the cases readily fall into three groups:

acute—operation within 48 hours of onset,
recent—operation within three weeks of onset,
old—operation at least three weeks after onset.

These groups are not only convenient from a chronological viewpoint, but constitute distinct entities in regard to clinical picture, leucocytosis, and prognosis.

In the acute group were 28 cases. Regardless of previous flowing and pain, the onset of

acute pain was usually marked by a recrudescence or augmentation of flowing. These patients are often in excruciating pain on admission. They have marked tenderness, seldom have palpable masses, but show a high degree of spasm and frequently shifting dullness. Signs of acute blood loss, such as air hunger, rapid pulse, perspiration and apprehension, are limited to this group of acute cases. They are markedly tender on vaginal examination unless unconscious. The white blood count is considerably elevated, varying from nine to 37,000, and averaging 18,200.

The recent cases were 32 in number. They present a history identical with the acute group except that the severe pain or collapse occurred longer ago than 48 hours and after it they had been confined to bed, limited in activity, or suffered milder exacerbations. Their acute symptoms have regressed but not disappeared. Spasm may remain, but shifting dullness is seldom present. Tenderness and residual soreness persist, and abdominal masses are more frequently palpable than in the acute group. These patients show evidences of chronic not acute blood loss; they may be weak and pale, and the flowing usually continues. They have vaginal tenderness usually localized to one vault or to the posterior culdesac, and most of them have definite pelvic masses. The white blood count is moderately elevated, averaging 11,300.

Twenty-two cases comprised the old group. History is essentially the same as in the other groups but longer removed from the present, hence more vague, the pain less severe and the correlation of pain with normal and abnormal menstrual flow quite indefinite. However, exacerbations of the less severe cramp-like pains continue, and the flow usually persists, diminishing somewhat in amount, perhaps merely staining. Several women entered with the chief complaint of vaginal bleeding of three months or more. Occasionally the normal menstrual cycle is entirely restored. Signs of pregnancy are seldom encountered in this group. Tenderness was usually present but not marked, and vaginal masses were felt in 77.7 per cent. Many of these patients complained of recent constipation, pain on defecating, frequency, dysuria, and other urinary symptoms. Those referable to the rectum were presumably due to the old pelvic hematoceles which were found on exploration. Even in this group the white blood count is slightly elevated, averaging 9,800.

Temperatures in both the acute and recent groups averaged 99.3°F., those in the old group 98.8°F. There appears to be no relationship between age of the process and the pulse, the gross average being 93, although one might expect an elevation in the acute cases.

RECAPITULATION OF GROUPS

	No. of cases	No. of missed cases	Per cent of missed cases
Acute	28	3	10.7
Recent	32	10	31.3
Old	27	11	40.7
Unruptured	3		
Total	90		

DIAGNOSTIC ERRORS

Correct Diagnosis made Pre-Op.	55 cases	61.1%
Correct Diagnosis included in Pre-Op. Diagnosis	11 "	12.2%
		73.3%
Correct Diagnosis not mentioned Pre-Op.	24 "	26.6%

Acute cases are the easiest to diagnose, only three being missed in this group. Ten were missed in the recent group, and 11 in the old. Thus 10.7 per cent of the missed diagnoses were acute, 31.3 per cent recent, and 40.7 per cent old. The older the case the more difficult the diagnosis. Analysis of the 24 missed diagnoses shows the following errors:

Salpingitis	6 cases
Pelvic Mass	6 "
Uterine Fibroids	4 "
Pelvic Inflammation or Abortion	1 case
Fibroid or Endometritis	1 "
Ruptured Viscus, probably Gall Bladder	1 "
Ovarian Cyst	1 "
Salpingitis or Ovarian Cyst	1 "
Uterine Pregnancy	1 "
Acute Intestinal Obstruction	1 "
Salpingitis or Acute Appendicitis	1 "

The list contains practically all of the usual misdiagnoses as well as two which seem rather remote. The case considered a ruptured gall bladder has been discussed above, and a correct diagnosis might have been reached if the initial pain and tenderness had been considered as criteria. The one case diagnosed acute intestinal obstruction simulated that picture perfectly, lacked premonitory pain, lacked bleeding, and showed an entirely normal vaginal examination. The preoperative diagnosis of intestinal obstruction was rectified upon feeling a mass in the left vault during ether examination—a valuable procedure. A few of the cases considered salpingitis might have been diagnosed correctly if more emphasis had been placed upon the profuse sanguineous discharge and signs of concomitant pregnancy, but this is one of the most excusable errors. Those cases which were operated upon without definite diagnosis other than pelvic mass were of the old group. They usually lacked signs of pregnancy, but continued flowing seemed to justify laparotomy.

DIAGNOSTIC AIDS

In the whole series the Aschheim-Zondek Test was used but once. Its more general application will somewhat improve the percentage of correct diagnoses although most of those missed fell in the older group in which the test would have already become negative. Sedimentation rate, posterior colpotomy, and frequent leucocyte counts as advocated by Farrar[2] should further reduce the diagnostic error.

MORTALITY

Three cases of the 90 died, a gross mortality of 3.3 per cent. All the deaths occurred in acute cases; one died of bronchopneumonia, 36 hours after operation, a second died 1½ hours after operation, apparently a circulatory death, and the third from septicemia due to a septic attempted abortion. In the second death the local physician must be held largely responsible. He saw the patient two hours after the onset of severe abdominal pain and collapse. The menstrual period was four days overdue, the physician did no pelvic examination but diagnosed indigestion and gave morphine. Another physician was summoned six hours later because of the patient's air hunger, pallor and anxiety. He was quick to recognize the signs of acute blood loss and immediately sent her into the hospital. Upon admission she was pulseless, had a blood pressure of 50/0, a red blood count of 1,500,000, and showed no localizing signs, probably because of the narcotic. Operation, transfusion, warm intraperitoneal infusion and other supportive measures were without avail, and she died within two hours after admission. Early recognition would in all likelihood have saved this patient.

DIAGNOSIS BEFORE RUPTURE

Having recognized the menace of ectopic pregnancy and the supreme importance of early diagnosis if possible before rupture or abortion, it is important to correlate the findings in the few cases seen prior to these events. Two cases were diagnosed positively and operated on before rupture or abortion, while two others ruptured during their stay on the wards, and one additional case was positively diagnosed, discharged against advice, and later ruptured in another hospital. Hence there are but five cases in the series upon which to construct the picture of intact extra-uterine pregnancy. They all present a history of sharp colicky pain in the lower abdomen varying from eight hours to one week. All of them had had some form of vaginal bleeding varying from one day to six weeks. All had localized abdominal tenderness although only one had a palpable mass. All had a bloody vaginal discharge at the time of examination and all were tender to vaginal palpation. One patient had a soft cervix, enlarged uterus and a history of amenorrhea, and another had a soft cervix, breast changes, and a history of morning sickness; these, highly suspicious cases, but the other three showed no signs of pregnancy whatsoever.

To summarize, then, vaginal bleeding, abdominal pain and tenderness, with or without the signs of pregnancy call for immediate pelvic examination. Localized vaginal tenderness, with a cervix painful to movement, renders the diagnosis probable, and evidences of concurrent pregnancy or a positive Aschheim-Zondek Test justify laparotomy.

SUMMARY

1. Ninety cases of extra-uterine pregnancy are reported in an attempt to evaluate the various signs and symptoms constituting a diagnosis.
2. The frequency of the various findings is tabulated.
3. Pain is almost invariably present; it is the most important single finding, and its locus of initiation is of considerable value if it can be accurately ascertained.
4. Bleeding per vaginam, abdominal tenderness, vaginal tenderness, and vaginal mass are the next most frequently observed, no other finding occurring in more than a third of the cases.
5. Signs and symptoms of pregnancy are comparatively rare in this series, and the diagnosis must frequently be made in their absence.
6. Division of the cases into three chronological groups: acute, recent, and old, is convenient and practical in regard to the clinical picture, leucocytosis, accuracy of diagnosis, and prognosis.
7. Most frequent mistaken diagnoses are salpingitis, uterine fibroids, and ovarian cysts.

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COMPLETE SURGICAL REMOVAL OF THE STOMACH FOR HOUR-GLASS DEFORMITY CAUSED BY CARCINOMA*

BY WILLIAM REID MORRISON, M.D.†

A PRELIMINARY report of the following case is presented as a successful total gastrectomy for scirrhous cancer. Until recently rather extensive cancer of the stomach has been considered inoperable, not only by the x-ray specialists, but also by the internists and general practitioners and surgeons. Modern surgeons, with increasing experience in gastric surgery, have successfully advanced from removing the distal portion of the stomach, to excision of a third, a half, three-quarters of that organ, or the whole stomach itself.

It is quite hopeful that under favorable conditions complete gastrectomy is a rational procedure, of course requiring adequate experience and operative technique.

Most surgeons interested in gastric carcinoma believe that patients with cancer of the stomach, diagnosed clinically and with confirming x-ray pictures, should be given the benefit of surgical exploration of the stomach, under favorable conditions, since one hundred per cent mortality faces the patient if he is treated medically.

The patient, Mrs. H., 53 years of age, a married Irish American housewife, was seen by the writer in consultation with Dr. Walsh on the First Medical Service of the Boston City Hospital on June 22, 1933. The chief complaint was gnawing pain in the upper abdomen and vomiting of six months' duration, with loss of weight of twenty-five pounds, loss of appetite, and weakness. The epigastric pain and distress occurred after meals but appeared almost any time during the day or night. Alkalies at first gave some relief. The anorexia and pain resulted in the patient's living on a liquid diet, but despite this simple diet she vomited. Constipation was noted, with tarry stools, and the patient states that she vomited blood once.

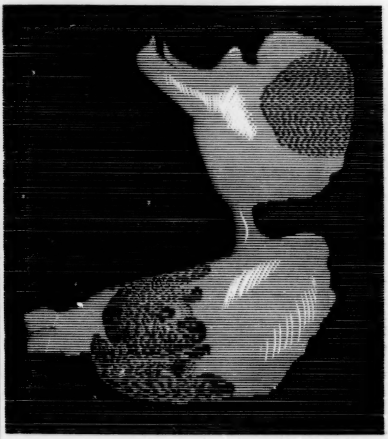
Physical examination revealed a somewhat emaciated woman, with a small hard freely movable mass in the epigastrium to the left of the midline, with some epigastric fullness and tenderness on palpation. Blood pressure was 110 systolic, 70 diastolic. Stools showed occult blood repeatedly. Temperature was 98°, pulse was 70, respiration 20. White blood count was 6200. Red blood count was 4,200,000. Hemoglobin was 70-75%. Non-protein nitrogen was 35. Kahn test was negative.

On June 16th Dr. Paul F. Butler reported the barium gastro-intestinal series as follows:

"Stomach is in median position. Peristalsis is irregular and sluggish. Stomach is freely movable and not tender. There is an hour-glass deformity of the stomach at the junction of the cardia and media. There is a filling defect of the antrum with irregularity on the lesser curvature side of the antrum. The sphincter was centric. No peristaltic waves passed over the lesser curvature of the antrum. The duodenal cap filled well and was regular in outline; the rest of the duodenum was negative. At six hours the stomach was empty and the head of the meal was in the transverse colon. The cecum was freely movable and not tender. The conclusions were old healed gastric ulcer at junction of cardia and media. Probable carcinoma of antrum. Barium enema was negative—the enema passed to the cecum without delay or obstruction. There were no irregularities, filling defects, tenderness or abnormal fixation of the colon."

The patient was placed on a convalescent Sippy diet for a week, then was transferred to the Second Surgical Service for operation which was performed on June 28.

Under gas-oxygen-ether anesthesia a six-inch right rectus incision was made in the right upper quadrant of the abdomen. The abdomen was explored and found to be negative except for the stomach which was involved in a mass extending from the pyloric region along the lesser curvature to the fundus. Several small lymph nodes were noted in the gastrocolic omentum, but these nodes were not enlarged. There was no evidence of metastases in the liver or elsewhere. The stomach was freely movable and was not adherent to the pancreas, but it was attached to the spleen by adhesions. A total gastrectomy was deemed the operation of choice. The first part of the duodenum was freed and a DePetz sewing clamp applied to it, then the duodenum was severed and the distal end infolded. Bleeding was controlled as the whole stomach was removed from below upwards to the esophagus, through which a duodenal tube had been inserted prior to operation. The stomach was then completely removed. The jejunum was carried through the transverse mesocolon and an end-to-side anastomosis was performed between the esophagus and the jejunum. The duodenal tube was then pushed down the esophagus and was threaded into the distal loop of the jejunum, and left in place. The great omen-



Hour-glass stomach with carcinoma in pyloric and cardiac areas, before operation.

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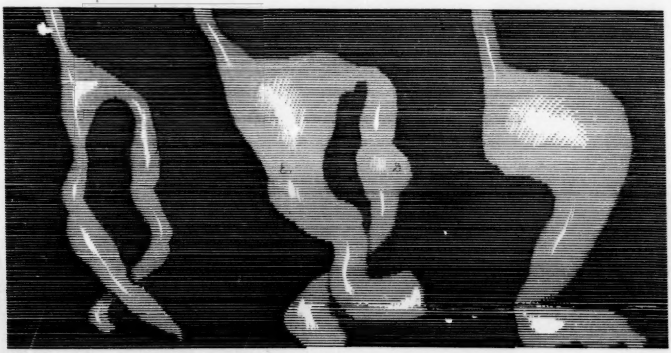
tum was sutured over the line of anastomosis and also over the inverted duodenal stump. The abdomen was sutured in layers without drainage.

Dr. Frank B. Mallory reported scirrhous carcinoma of the stomach.

The patient had an uneventful convalescence except for some diarrhea. She was up and about the ward on the nineteenth day after operation and was discharged to her home on July 31. Patient's weight after operation was 110 pounds. Since then after indiscretions in diet she has regurgitated food and bile at times. Her weight now varies from 100 to 110 pounds. Fluoroscopic examination on July 29th, a month after operation, revealed the barium passing promptly and freely directly from the esophagus into the distal loop of the jejunum which was observed to be contiguous with the esophagus. Subsequent x-ray examination in October revealed dilatation of the jejunum at site of anastomosis, but no evidence of obstruction.

The patient now has a mild secondary anemia, with hemoglobin of 68%, red blood count of 4,000,000. She has been taking iron and ammonium citrate and diluted hydrochloric acid since operation. She has not developed pernicious anemia.

A B C



A and B represent anastomosis of esophagus and jejunum one month after operation.
C represents dilatation of jejunum two months after operation (side view).
D represents proximal loop of jejunum.
E represents distal loop of jejunum.

SUMMARY

1. A case is presented of successful operative removal of the whole stomach for scirrhous cancer involving the cardiac and pyloric portions of that organ, as well as the lesser curvature, with hour-glass deformity.

2. The jejunum was carried up behind, rather than in front, of the colon through the transverse mesocolon, and an end-to-side anastomosis was made between the esophagus and jejunum.

3. A duodenal tube was inserted through the nose and down the esophagus into the stomach before operation, and was left in place. Before removing the entire stomach, the tube was pulled out of the nose so that the distal end of the tube left the stomach and could be felt in the lower end of the esophagus. On making the end-to-side anastomosis the tube was threaded into the distal loop of jejunum.

4. The abdomen was closed without drainage.

5. Liquids were given by mouth and through the duodenal tube 24 hours after operation, instead of the usual starvation period of four to fourteen days.

6. Mild secondary anemia with no evidence of pernicious anemia was controlled with iron and ammonium citrate two capsules of 15 grains each t.i.d. without giving liver or liver extracts. Dilute hydrochloric acid 15 drops t.i.d. was given in water to control the usual diarrhea which follows total stomach removal.

7. With further progress in gastric surgery, more complete gastrectomies will undoubtedly appear in the literature.

SPONTANEOUS INTRAPERITONEAL HEMORRHAGE OF UNKNOWN ORIGIN COMPLICATING PREGNANCY

(Report of Two Cases)

BY EMILIO D'ERRICO, M.D.*

INTRAPERITONEAL hemorrhage may occur from several well-established causes. Chief among these is the intraperitoneal hemorrhage of pelvic origin due to ruptured ectopic pregnancies, rupture of the pregnant uterus, and rupture of corpora hemorrhagica. Less frequent, but by no means uncommon is the intraperitoneal hemorrhage due to traumatic rupture of organs, especially of the liver, spleen, and kidney. Last, there are the rare causes of spontaneous intraperitoneal hemorrhages due to rupture of diseased spleen, rupture of pelvic varices, rupture of small vessels associated with fibroids of the uterus and mesenteric thrombosis; occasionally, intraperitoneal hemorrhage is found as a manifestation of hemorrhagic diatheses.

Spontaneous intraperitoneal hemorrhage has been recorded by Whipple and Sperry[1] in dogs, in which the hemorrhagic disease had been produced artificially by chloroform poisoning. Peck[2] has described a case of "Toxic Hemorrhagic Hepatitis" with intraperitoneal hemorrhage in a man, 23 years old, who had been operated on for appendicitis. Barber[3] has reported a case of extensive intraperitoneal hemorrhage in a woman following labor, for which no source could be found. Frank[4] has reported a case, the third of its kind he had encountered, where on opening the abdomen, a large intraperitoneal hemorrhage was found, the source of which was never determined. Harrigan, Broun and Vineberg[5] have independently reported cases of severe intraperitoneal hemorrhage of unknown origin. Churchman[6] reported another case, giving autopsy findings which, however, did not throw much light on the source of the bleeding.

In a fairly complete search of the literature, I have been unable to find any reports of cases of intraperitoneal hemorrhage of unknown origin complicating pregnancy. The following two cases are therefore reported because of their unusual character, and also in the hope that they may encourage more reports, further data and study of this serious complication of pregnancy.

CASE 1. On December 28, 1932, I was asked by Dr. J. W. Gahan to see at her home, Mrs. A. A., primigravida, 24 years old, married two years, and at that time about five and a half months pregnant. Without any apparent reason, five hours previously, the patient had collapsed, remaining more or less unconscious for 15-20 minutes, following which she had complained of headache, tired feeling and of a severe, dull and continuous pain in the lower abdomen, more marked in the right lower quadrant, and increased by several vomiting spells. Physical examination showed a rather pale but fairly well-nourished young woman, in bed, conscious and rational. Her mucous membranes and conjunctivae were somewhat anemic in appearance. The abdomen was rather full and doughy. The uterus rising to the level of the umbilicus was easily mapped out, and found symmetrical and smooth. There was moderately diffuse tenderness throughout the abdomen, but definitely more distinct in the region of an old appendectomy scar. This region was also marked by a slight, but definite muscle spasm; there was no costovertebral tenderness and no shifting dullness. The fetal heart was heard distinctly over the L. L. Q. Vaginal examination disclosed a soft cervix with its external os closed; ballottement present; uterus the size of a five to five and a half months' pregnancy, regular in outline and soft. There was no evidence of external bleeding. Both vaults were free. Pulse 84, temp. 97.6°, resp. 22, B. P. 90-60, urine examination negative except for a very slight trace of albumin.

Although no definite diagnosis was made, my impression was that the collapse had probably been caused by a subacute torsion of some organ, the evident improvement in the patient's condition pointing to spontaneous relief. Hot fomentations to the abdomen, morphia gr. ¼ s.c. and close observation were recommended.

Four or five days later I was told by Dr. Gahan that the patient was up and about, but she still complained of some distress in the R. L. Q. and her vomiting, although to a lesser degree, persisted.

On the evening of January 10, 1933, the patient collapsed again. Dr. Gahan, having found her in shock, advised hospitalization and referred her to the Lawrence Memorial Hospital, in Medford, Massachusetts. On admission the pulse was 88, the temperature 97.4°, and the B. P. 60-30. Under heaters, extra blankets and elevation of the foot of the bed, the general condition improved temporarily. She vomited several times. Two hours later once again she sank into shock. I saw her at 2:45 A.M. on January 11. The patient was extremely pale, semiconscious, but could be aroused. Pulse 128, temp. 97.4°, resp. 24. Skin cold and clammy. Abdomen full, tender throughout, especially over the old appendectomy scar. Shifting dullness present. Uterus symmetrical and soft, fundus just above the umbilicus; fetal heart over L. L. Q., rate 144, good rhythm. Hemoglobin 80%. Catheterized urine was negative but for a very slight trace of albumin.

Exploratory Laparotomy: Incision through the old right pararectus scar. On opening the peritoneal cavity, a large amount of free and clotted blood, estimated to about one quart, welled out of the wound. To facilitate exploration, the incision was carried well up into the R. U. Q. The uterus corresponded to the size of a five to a five and a half months' pregnancy, pale blue, soft, and its wall was intact; both tubes, ovaries and broad ligaments normal in appearance and presented no bleeding point. An old, brownish clot was removed from an old omental adhesion at the site of the appendectomy scar, but there was no bleeding point. The posterior cul-de-sac, except for the presence of recent blood clots, was perfectly clear. Exploration of the bowel, omentum and mesentery gave no evidence of bleeding areas. A very large, recent blood clot was removed

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from the anterior and under surface of the liver, but visual exploration failed to reveal the source of the hemorrhage. The liver seemed to be smaller and paler than normal, but its capsule was smooth and did not present any evidence of abnormality. The gall bladder and the stomach were also negative. Manual exploration in the region of the spleen disclosed a very large blood clot which filled the cavity of both hands, but no bleeding point was found. Working on the possibility that the bleeding might originate from a spontaneous rupture of the spleen, and not being satisfied by a negative manual exploration of that organ, the laparotomy wound was closed, and the abdomen reopened by a high left pararectus incision. The spleen was found normal in size and color, and its capsule was found intact. As further exploration failed to throw light on the possible cause of the hemorrhage, the abdomen was closed. Two thousand cc. of salt solution were given subpectorally during the operation, and the patient was returned to bed in fair condition. Two hours later, 500 cc. of citrated blood were transfused with some improvement in her general condition. At 10:00 A.M. the patient, once again giving evidence of shock, was again transfused with 300 cc. of citrated blood. Improvement again was noted; this time, however, of shorter duration. The pulse became imperceptible, the respiration became Cheyne-Stokes in character, and she died nine hours after operation.

Permission for an autopsy was refused.

CASE 2. (I am indebted for this case to Dr. G. E. May, who operated on this patient at the Newton Hospital, Newton, Massachusetts. Dr. May's notes are given unedited.)

Mrs. E. B., secundigravida, 32 years old, was admitted to the Newton Hospital on September 30, 1929. Admission No. 82250.

P. H. Cesarean Section in October, 1927.

P. I. On September 30, 1929, at 9:00 P.M. the patient had a sharp epigastric pain which caused her to double up. The pain persisted, and only partial relief was obtained by ½ gr. of morphia. She was brought into the hospital and I was asked to see her in consultation. R. B. C. 2,400,000, hemoglobin 41%, B. P. 102-60.

P. E. All negative except for abdomen.

Abdomen: Extremely tender all over with very little true spasm and no involuntary rigidity. Fundus palpable four fingers above the umbilicus. Diagnosis of probable ruptured uterus with intraperitoneal hemorrhage was made and operation advised.

Laparotomy: On opening the abdomen, 600-800 cc. of fresh blood was found in the abdominal cavity. The seven months' uterus obscured exploration. Because of the previous cesarean, a classical section was done uneventfully. The uterus reacted well. The placenta was attached over the posterior upper wall and over the left cornu. The uterine incision was then sutured and the uterus drawn out of the abdomen. Both tubes and ovaries were normal. Some varices of both broad ligaments were present, but no bleeding point was found. Two small purplish nodules on the back of the right broad ligament resembling endometrial implants were found, but no bleeding was seen there. The omentum and appendix were negative. The spleen was negative. The liver, gall bladder and stomach were also negative. No bleeding point was found anywhere in the abdomen. The abdomen was closed in layers without drainage. Uneventful postoperative convalescence. The patient was discharged well on October 17, 1929.

COMMENT

The absence of recorded cases of spontaneous intraperitoneal hemorrhage complicating pregnancy indicates the extreme rarity of this condition. Speculations as to the probable etiological factors for the intraperitoneal hemorrhage of our two cases might perhaps be directed to the liver, which, because of its apparent small size, may have been the seat of toxic atrophic changes. In the second case, a premature separation of the placenta, with escape of blood through the right tube might be regarded as a compatible explanation. The author would welcome any data on the subject.

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THE EFFICACY OF METHENAMINE AS A BACTERICIDAL AGENT IN URINARY TRACT INFECTIONS*

BY VINCENT VERMOOTEN, M.D.,† AND REGINALD V. BERRY, M.D.†

Introduction.

THE treatment of urinary tract infections still remains one of the main problems of the urologist and not at all a satisfactory one for the general practitioner. Evidence of this is the gradually increasing number of drugs manufactured for this purpose which are constantly appearing on the market and reports in the literature on the efficacy of these drugs as bacteriostatics and bactericides.

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Methenamine, although prepared by Butlerow[3] as long ago as 1860 and introduced as a therapeutic agent in vesical conditions by Nicolaier[12, 13] in 1894, is probably still our most efficacious urinary antiseptic and beyond question of doubt the one most commonly used. Helmholz and Field[8] in carefully controlled experiments on rabbits with colon bacillus infection of the urinary tract were able to cause the urine to become "sterile" when 0.5 Gm. of Methenamine was given twice a day while the urine was kept at an acidity of pH 4.5 to pH 5.5 by means of a diet of oats, bread and water. Rabbits similarly infected with B. coli were given mercurochrome, 0.2 Gm. daily. These rabbits

showed a definite decrease in the degree of infection but cultures never became entirely negative. With 0.5 Gm. of hexylresoreinol daily there was relatively little change in the severity of the infection as determined by culture of the urine. These results would tend to indicate that despite later observations by other investigators[19], methenamine is probably, at the present time, our most efficient urinary antiseptic.

THE LIBERATION OF FORMALDEHYDE FROM HEXAMETHYLENAMINE

In 1899 Nicolaier[14] demonstrated formaldehyde in the urine as a split product of hexamethylenamine. In 1913 Hinman[9], Hanzlik and Collins[6] and others showed definitely that an acid urine was necessary for formaldehyde to be liberated in the urine. The more acid the urine, the more formaldehyde was liberated. This reaction, which is reversible, takes place according to the following equation:—

$$(CH_2)\ 6N_4 + 6H_2O \rightleftarrows 4NH_3 + 6HCHO$$

hexamethylenamine + water ⇄ ammonia + formaldehyde

The unfortunate fact, however, is that the same degree of acidity does not always yield the same amount of formaldehyde. Thomas and Wang[19] found that "there were cases when the urines were highly acid and yet the formaldehyde content was comparatively low. This, as estimated by the Rimini method, is probably due to the fact that the formaldehyde content does not necessarily bear a direct relation to the antiseptic strength of the particular urine." Hinman[9] explains this on the ground that formaldehyde, in some cases, will combine with organic and inorganic substances in the urine and the resulting by-products have practically no antiseptic value. Nicolaier[15] mentions the fact that hexamethylenamine unites with uric acid to form a very soluble diformaldehyde uric acid, while Hammarsten[5] and Cammidge[4] both state that when formaldehyde is added to urea a combination takes place. Shohl and Deming[17], on the other hand, have shown in vitro and also in vivo that there is a very definite relation, in most instances, between the true acidity of the urine and the amount of hexamethylenamine which is converted into formaldehyde. They found that at pH 5.0 20 per cent of the hexamethylenamine was converted into formaldehyde; at pH 5.4 13 per cent, at pH 5.8 8 per cent, at pH 6.4 only 3 per cent, and none at all at pH 7.6.

THE FORMALDEHYDE CONCENTRATION IN THE URINE

(a) *Review of the Literature.* Levy and Strauss[11] in their determinations were able to obtain a formaldehyde concentration in the urine of 1:5,000 when giving their patients 7.5 gr. of hexamethylenamine three times a day. Burnam[2], giving 5 gr. to 10 gr. three times a day, was also able to get a concentration of formaldehyde of 1:6,000 which is the greatest concentration that Thomas and Wang[19] got using 15 gr. three times a day.

(b) *Experimental.* Thinking that a larger quantity of hexamethylenamine might result in a greater concentration of formaldehyde in the urine, we gave several patients 25 gr. to 30 gr. of hexamethylenamine with 15 gr. to 20 gr. of sodium acid phosphate three times a day for varying periods of time. We were able to get a concentration of 1:4,000 twice in one patient whose urine was examined every day for thirty-four consecutive days and during three of these days every urine specimen voided was examined. In this same patient the urine reached a concentration of 1:5,000 only eight times in fifty-seven determinations. In this patient, as well as in our other patients studied, a formaldehyde concentration of 1:6000 and 1:8,000 was not at all uncommon, but in the others a concentration of greater than 1:6,000 was only once obtained. All these patients had their total fluid intake limited to 1,200 cc. per day and the urine examined was the early morning specimen which was therefore the most concentrated, the most acid, and had been in the bladder over the longest possible period of time.

The first patient was given hexamethylenamine 25 gr. and sodium acid phosphate 15 gr. three times a day. The fluid intake was reduced to 1,000 to 1,200 cc. per twenty-four hours. On the nineteenth day the hexamethylenamine was increased to 30 gr. and the sodium acid phosphate to 20 gr. three times a day. The treatment was discontinued on the thirty-fourth day when gross blood appeared in the urine. One other patient developed hematuria on the twenty-seventh day of the treatment. Table I

TABLE I

THIRTY-FOUR DAY COURSE OF HEXAMETHYLENAMINE TREATMENT IN A CASE OF URINARY INFECTION

Day	Concentration of Formaldehyde	Day	Concentration of Formaldehyde
1	1:10,000	18	1: 8,000
2	1: 8,000	19	1: 5,000
3	1:10,000	20	1: 6,000
4	1: 8,000	21	1: 6,000
5	1:20,000	22	1:12,000
6	1:10,000	23	1: 6,000
7	1:12,000	24	1:10,000
8	1: 8,000	25	1: 8,000
9	1:10,000	26	1: 4,000
10	1: 6,000	27	1: 8,000
11	1: 8,000	28	1: 5,000
12	1: 8,000	29	1: 4,000
13	1:10,000	30	1: 6,000
14	1: 6,000	31	1:10,000
15	1:20,000	32	1: 5,000
16	1: 6,000	33	1: 8,000
17	1: 6,000	34	1: 6,000

(Specimens were collected aseptically by catheterization at 9:30 A.M. each morning. The urine was examined within the following hour.)

NOTE: All these determinations were made according to the Hanzlik and Collins[7] modification of the Jorissen method.

gives the details of the experiment on the first patient which is typical for all the patients studied.

On the twenty-seventh, twenty-eighth, and twenty-ninth days of the experiment every specimen of urine passed by the patient was examined for formaldehyde concentration. These results are recorded in table II.

TABLE II

Time	Urine	Concentration of Formaldehyde
Jan. 13		
1:00 P.M.	20 cc.	1: 6,000
2:20 "	30 cc.	1: 8,000
4:35 "	60 cc.	1: 8,000
5:30 "	60 cc.	1: 5,000
6:40 "	60 cc.	1: 8,000
8:05 "	60 cc.	1:10,000
9:25 "	60 cc.	1:10,000
10:30 "	60 cc.	1:12,000
Total	410 cc.	
Jan. 14		
5:30 A.M.	10 cc.	1: 6,000
7:30 "	30 cc.	1:20,000
8:30 "	35 cc.	1:20,000
Catheterized	20 cc.	1: 5,000
10:30 A.M.	40 cc.	1: 6,000
11:20 "	50 cc.	1: 8,000
12:50 P.M.	45 cc.	1: 6,000
2:40 "	30 cc.	1: 5,000
3:15 "	40 cc.	1: 5,000
4:15 "	30 cc.	1: 6,000
5:15 "	25 cc.	1: 8,000
6:30 "	40 cc.	1: 6,000
7:30 "	30 cc.	1: 5,000
Total	425 cc.	
Jan. 15		
1:45 A.M.	30 cc.	1:12,000
4:00 "	30 cc.	1:20,000
7:35 "	50 cc.	1: 4,000
9:25 "	30 cc.	1: 6,000
Total	140 cc.	

BACTERIOSTATIC AND BACTERICIDAL PROPERTIES OF FORMALDEHYDE

(a) *Introduction.* In the first of the three cases studied the only effect of the hexamethylenamine on the organisms was that the B. coli was modified. It took the Gram stain very poorly and the colonies were pinpoint rather than the typical broad B. coli colonies.

According to most authorities these samples of urine ought to have been completely bactericidal, but strangely enough they were not. It was always possible to grow organisms from these urines in beef broth and microscopically they always contained pus cells and bacilli.

The work of Helmholz and Field[8] led us to think that their anomalous findings of negative urine cultures, when autopsy showed multiple renal abscesses, were due to the bactericidal or bacteriostatic effects of the formaldehyde present in the urine. One of us[20] showed a marked discrepancy between the microscopic examination of the freshly obtained urine specimen and the culture report. These findings have subsequently been confirmed by Seidman, Ellis and Hill[16] and also by Baker[1]. At that time the suggestion was made that some of the discrepancies might be due to the bacteriostatic or bactericidal properties of the urine following the ingestion of urinary antiseptics.

(b) *Review of the Literature.* Reviewing the literature on the subject we find that Hinman[9] says, "In order that formaldehyde in the urine may be of clinical value urine should contain a strength of at least 1:30,000. The best effect will be procured with a germicidal strength or a solution of 1:6,000."

Levy and Strauss[11] claim that to be of any value formaldehyde should be in the bladder in strength of 1:5,000 to 1:15,000 while to be of bactericidal value it should be present in concentration of 1:1,000 to 1:5,000.

Hanzlik and Collins[6] state that "the limit of bactericidal efficiency in general is from 1:10,000 to 1:5,000 for a majority of organisms."

Thomas and Wang[19] in their careful study conclude "formaldehyde in aqueous solution will inhibit staphylococcus aureus in 1:20,000 and B. coli in 1:15,000 and completely destroy both in 1:5,000. Urine as a diluent reduces the antiseptic strength for the respective organisms to 1:15,000 and 1:10,000 dilutions and the germicidal strength to 1:7,000 and 1:5,000 dilutions.

Further, Shohl and Deming's[17] chart showing the bactericidal and bacteriostatic properties of formaldehyde confirms the observations of the authors above mentioned. Their results seem to prove that "in urine, at body temperature, a concentration of formaldehyde of 1:5,000 to 1:10,000 kills eighty to eighty-eight per cent of the organisms in two hours and one hundred per cent in twenty-four hours."

(c) *Experimental.* If these observations were correct then our patients should have shown some very definite improvement, especially the patient who only twice during thirty-four consecutive days had a formaldehyde concentration as low as 1:20,000. During the other thirty-two days it was 1:10,000 or greater, mostly 1:6,000 to 1:8,000. Accordingly we repeated this part of Shohl and Deming's work in detail and obtained very similar results, viz.,

TABLE III

PER CENT B. COLI "KILLED" IN URINE AT 37°C BY FORMALDEHYDE

	1:5,000	1:10,000	1:20,000	1:40,000
15 min.	52	18	8	0
1 hour	73	62	28	0
2 hours	85	78	60	16
24 hours	100	100	0	0

(The concentration of formaldehyde is indicated by the fraction at the top of the columns. The per cent killed was calculated with reference to the number of organisms growing in urine containing no formaldehyde.)

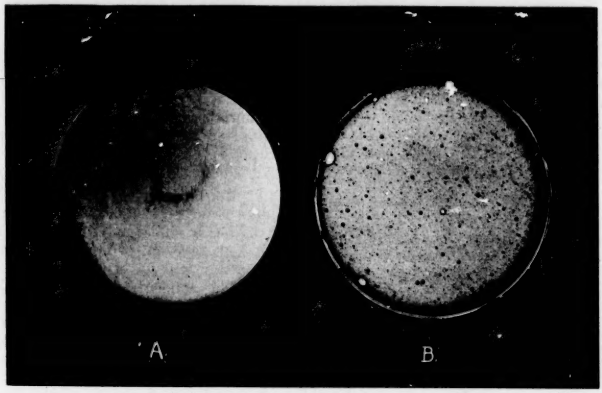

FIG. I. Photograph of agar plates. In each instance a forty-eight hour bouillon culture of B. coli was allowed to incubate for half an hour at 37° C. in sterile urine and enough formaldehyde to make a concentration of 1: 3,000. In "A" one cubic centimeter of this culture was plated in agar and incubated for twenty-four hours while in "B" a similar one cubic centimeter sample of the same culture was first centrifuged to remove the formaldehyde present in the culture medium and then taken up in saline and plated in agar.

Note how in "A" the impression is gained that the organisms had all been killed by being allowed to be in contact with a 1: 3,000 solution of formaldehyde for half an hour. "B" shows that the action of the formaldehyde was merely bacteriostatic and not bactericidal.

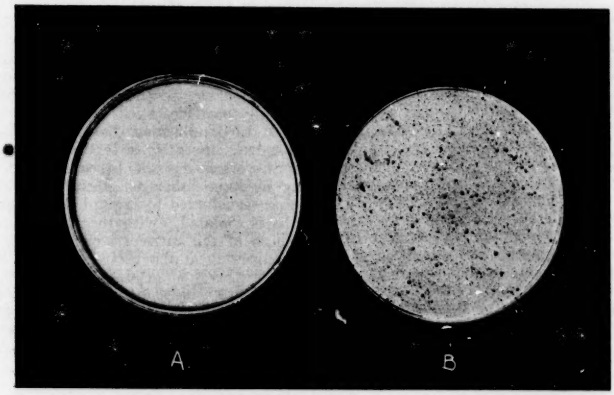

FIG. II. Photograph of agar plates in an experiment similar to that shown in figure I except that here the colon bacilli were incubated at 37° C. in the presence of a 1: 3,000 solution of formaldehyde for three and one-half hours instead of only half an hour. "A" is again the uncentrifuged specimen and "B" the centrifuged.

NOTE: This is a concentration of formaldehyde greater than can ever be obtained in the bladder urine. The time of incubation is the maximum that urine can ordinarily be retained within the bladder.

These surprising results caused us to repeat the above experiments using only the 1:5,000 concentration of formaldehyde. This time, however, two one cubic centimeter samples were removed at half hour intervals for three and one half hours. One sample was centrifuged to free the bacilli from the formaldehyde in which they were suspended. This specimen was then taken up in bouillon extract and plated. The other one cubic centimeter sample was plated exactly as before. The results are shown in table IV.

TABLE IV

PER CENT B. COLI "KILLED" IN URINE AT 37°C BY A 1:5,000 SOLUTION OF FORMALDEHYDE

	Uncentrifuged	Centrifuged
½ hour	61	0
1 hour	73	0
1½ hours	78	0
2 hours	81	0
2½ hours	84	0
3 hours	89	0
3½ hours	96	0

The centrifuged one cubic centimeter specimens plated at half hour intervals showed no reduction in the number of colonies over the three and one half hour period.

The experiment was again repeated, this time using eight cubic centimeters of freshly voided sterile urine, five cubic centimeters of the 1:1,000 formaldehyde solution and two cubic centimeters of a forty-eight hour bouillon culture of B. coli. The results are shown in table V.

TABLE V

PER CENT B. COLI "KILLED" IN URINE AT 37°C BY A 1:3,000 SOLUTION OF FORMALDEHYDE

	Uncentrifuged	Centrifuged
½ hour	100	0
1 hour	100	0
1½ hours	100	0
2 hours	100	0
3 hours	100	0
3½ hours	100	0

The centrifuged one cubic centimeter specimens plated at half hour intervals again showed no reduction in the number of colonies over the three and one half hour period (figs. I and II).

(d) *Discussion.* Apparently the "unwashed" organisms did not grow for the obvious reason that they were inoculated with formaldehyde into agar, and it was this formaldehyde that prohibited their growth in agar just as it had in the original solution.

Although these findings are contrary to those of most other investigators who have made observations along these lines, we find that in 1911 Kendall and Edwards[10] in an article on "a new method for determining the germicidal value and penetrating power of liquid disinfectants" found by their method, among other things, that exposing a culture of B. coli for three hours at 20°C to a 1:400 solution of formalin and then incubating for seventy-two hours at body temperature, they still obtained a growth of the organisms. They were, however, all killed after a five hour exposure.

This substantiates our finding that a 1:3,000 solution of formaldehyde has no bactericidal effect on a twenty-four hour culture of B. coli even after three and one half hours of exposure at 37°C.

CONCLUSIONS

(1) Concentrations of formaldehyde in the bladder urine up to 1:6,000 can be obtained when the urine is sufficiently acid and the patient takes 5 gr. to 10 gr. of hexamethylenamine three times a day and has a limited fluid intake.

(2) The concentration of formaldehyde remains the same when patients are taking 15 gr. (1 Gm.) three times a day, but when the dose is increased to 30 gr. (2 Gm.) three times a day the concentration is occasionally as great as 1:4,000 to 1:5,000 when the fluid intake has been limited to less than 1,500 cubic centimeters per twenty-four hours and the urine is sufficiently acid.

(3) Large doses of hexamethylenamine—90 gr. (6 Gm.) a day—taken for periods greater than three or four weeks may cause gross hematuria.

(4) It is therefore unnecessary to give hexamethylenamine in doses greater than 7.5 gr. three times a day provided the fluid intake is limited and the urine sufficiently acid, as this will allow the development of a bacteriostatic urine in the bladder.

(5) Formaldehyde in strengths greater than can be obtained in the bladder urine (1:3,000) incubated with B. coli for three and one half hours (the equivalent of accumulating urine in the bladder for seven hours) is not bactericidal but only bacteriostatic.

(6) In determining the bactericidal property of a drug, the drug, after being allowed to act on the organisms should be removed by washing or some other satisfactory method before being transferred to agar plates for culture, for if it is "plated" with the drug there may be enough of the antiseptic carried over with the organisms to inhibit their growth on agar.

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THE STATUS OF VASOGRAPHY*

BY EDWARD A. EDWARDS, M.D.†

INTRODUCTION

THE roentgenologist gives the surgeon diagnostic data of prime importance in the study of almost every tissue and system in the body. The advances made in the visualization of the gall bladder, the lung, and the spinal cord have been so universally adopted as to render them almost commonplace. The only system partaking but sparingly of these advances is the vascular. In most clinics, the state of the arteries and veins not actually subcutaneous is still determined by methods yielding presumptive data, rather than by actual visualization. Thus, we may judge of the patency of the deep veins of the leg by noting whether superficial varices present will empty quickly, when the superficial return is occluded by a tourniquet; or in gangrene of the foot, we may decide on the state of the deep arteries and the level of their occlusion by the degrees of circulatory insufficiency in the skin of the limb. Present satisfaction with the diagnostic methods used, however, does not negate the undoubted benefit of accurately visualizing the diseased vessels.

Finding the ideal contrast medium with which to visualize the blood vessels in the living patient has been difficult. Such a medium must satisfy all the following requirements to be universally applicable:

1. It must be satisfactorily opaque, even when diluted to some extent by the blood.
2. It must be freely miscible with the blood and not give embolism or false filling defects in the roentgenogram.
3. It must be sufficiently limpid to be able to be introduced into the vessel quickly and through a needle small enough to enter without undue damage.
4. It must not injure the blood chemically, i.e., not give coagulation or hemolysis.
5. It must not irritate the blood vessels sufficiently to give thrombosis through intimal damage, or endanger an already anemic limb through additional vasospasm.
6. Its accidental escape outside the blood vessel should not cause severe inflammation.
7. It must not have a toxic effect on the organism, exclusive of the blood or blood vessels.
8. Its use must not be so painful as to necessitate a general anesthetic.
9. It must not be appreciably altered by adequate sterilization.

COMPARISON OF VASOGRAPHIC MEDIA

The history of vasography is concerned with the finding of such a medium. Trendelenburg in 1902 was probably the first to describe an opaque substance within the circulating blood[1]. His patient had been shot in the heart. On x-ray, the shot could be seen in the heart, being agitated to and fro by the moving blood. In 1903, Riethus described the x-ray appearance of movements of shot and other foreign bodies introduced into the hearts of dogs by way of the jugular vein[2].

The first experiments with a liquid medium were done in 1910 by Franck and Alwens, in dogs and rabbits[3]. They used a suspension of bismuth in oil, introduced into the heart directly or via the large veins. They then followed the course of the drops of this suspension through the heart chambers and into the lungs. In the same year, Schepelmann[4] reported experiments on rabbits and frogs, in which he had tried solutions of the heavy metals as well as oil suspensions. He discarded the oily suspensions as being too dangerous from the standpoint of embolism, and the salts of the heavy metals as being too toxic in the strength necessary to cast good shadows.

The earliest good vasograms of the living person that I have seen were published in 1923 by Berberich and Hirsch[5]. They used a ten to twenty per cent solution of strontium bromide, and their pictures are fairly clear. In 1924, Brooks of this country published good arteriograms of the leg made after the injection of sodium iodide. He used a solution made by dissolving 100 grams of the crystals in 100 cc. of water, i.e., a 50% solution, by weight. (Brooks, B.: Intra-arterial injection of Sodium Iodide. *J. A. M. A.* 82:1016, 1924.) Later, in 1929, Charbonnel and Massé[6] after considering the iodides and bromides of strontium, sodium

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and calcium, chose sodium iodide as the best substance, and obtained good visualization of the arteries, but mentioned the irritating effect of this substance.‡

We have in our newer materials, I believe, substances of better contrast and less irritating

FIG. 1. Comparative opacities of radiographic solutions. These solutions were enclosed in rubber tubes and all laid on a single x-ray plate and the exposure made. From left to right: 1. 50% Strontium Bromide. 2. 20% Sodium Iodide. 3. Iodochlorol Emulsion. 4. Thorotrast.* 5. 40% Skiodan. 6. 35% Neo-Skiodan.

action than either strontium bromide or sodium iodide. I have used twenty per cent sodium iodide in twenty cc. doses, but this drug is painful when introduced quickly, and I have seen in one case a phlebitis leading to a complete and permanent sclerosis of the injected vein. The contrast was poor. Of course, where the blood current is rapid, a phlebitis or arteritis would occur only with a solution of even more irritating qualities, as the solution becomes quickly diluted. Where the blood flow is sluggish, however, as in varicose veins, or narrowed end arteries, or in normal vessels isolated by the tourniquet, a twenty per cent sodium iodide solution may do harm.

The wide use of iodized oil (lipiodol) has led to its trial in the visualization of both arteries and veins. Sicard and Forestier in their early experiments (1923) injected lipiodol without any harm into the femoral vein and carotid artery of the dog[7]. Later (1927) Carnett and Greenbaum published fairly good arteriograms of the lower limbs of living patients,[8] using lipiodol in quantities up to six cc. Its oily nature, however, has prevented its fully satisfactory use. Being non-miscible with blood, it prevents the danger of fat embolism. Further, one cannot tell whether a roughening or filling defect seen in an arteriogram is a projection of the vessel wall or merely blood not completely displaced by the lipiodol. Once having been pushed distally by the blood stream, it may block end vessels, and where the circulation is sluggish, as in cases with impending gangrene, the blood flow may not be sufficiently forceful to dislodge the oil for some time, leaving the regional tissue anemic. No investigator has dared, therefore, to use sufficient lipiodol actually to fill the vessel, the only way to get good vasograms. Furthermore, lipiodol is too viscid to be introduced quickly through a fine gauge needle, and more damage is therefore done to the vessel wall than where a limpid solution is injected through a fine needle.

These disadvantages have to some extent been removed by the process of emulsifying the lipiodol. In 1930 Saito et al[9] reported on the use of such an emulsion, made with the aid of "protalbin-albumin acid", lecithin, and glucose. They used as high as twenty cc. of this emulsion in each patient, in various arteries, including the carotid, femoral, and brachial. Their vasograms are very clear, with good detail, and they reported no untoward local or general effects. It is hard, however, to overcome a very logical feeling against the intravascular introduction of an oil, however well emulsified it is said to be. This type of medium remains, however, as one deserving of further use and observation.

I wish now to consider a solution being widely used, but which I believe has, at present, no justification for wide clinical use. This preparation, "Thorotrast" consists of a twenty-five per cent aqueous solution of thorium dioxide with the addition of a colloidal substance said to be of a carbohydrate nature. It was introduced by Radt in 1930 for the delineation of liver and spleen[10]. It can be injected into a vessel without pain or local deleterious effect. Once in the blood stream the thorium dioxide is absorbed by the cells of the reticuloendothelial system. In the liver and spleen it casts sufficient shadow to give good pictures of these organs on the roentgenogram. Thorotrast was first reported on as an arteriographic medium in 1932 by Moniz et al[11], who obtained good visualization of the carotid distribution in the head. Dos Santos et al[12] reported on its use in vasography in over forty patients without untoward effect; and obtained very excellent pictures of the vessels. They state: "We consider that, thanks to Thorotrast, the practical problem of arteriography of the limbs, without danger or pain, is definitely resolved." Later in the same year, Allen and Camp of the Mayo Clinic published an enthusiastic report on arteriography with Thorotrast[13].

Thorotrast is the most opaque of all the media we now possess. (Figure 1.) The report of the Council on Pharmacy and Chemistry of the American Medical Association, on Thorotrast, is, however, replete with warnings of its toxicity[14]. In the first place an immediate reaction may occur after its injection, including slight to moderate febrile reaction; vomiting in hepatic cirrhosis; anaphylactoid reactions; hematemesis in patients with gastric ulcer or malignancy, and moderate and transient anemia. Its early effect on the spleen may result in acute splenitis, as reported in four cases by Stewart, Einhorn and Illick[15]. R. Lewisohn reports severe nuclear damage in both liver and spleen[15]. Aside from these untoward effects, which are reduced to a minimum in vasography, where one can use less than the 75 cc. total dosage recommended for hepatolienography, the radioactivity of the thorium held

‡The proteinated silver salts have been tried, especially in Germany, but their contrast is poor and the danger of argyria is evident.

*Supplied by the manufacturers, Heyden Chemical Corporation.

in a more or less permanent combination throughout the reticulo-endothelial system comprises a menace of unknown proportion. So far as the present state of knowledge goes, its radioactivity may be intensified with its slow chemical deterioration and therefore may not show its deleterious effects till years have elapsed. It is this "ultimate toxicity" of thorium that is still sufficiently unknown, that renders this drug unfit for wide clinical use. As H. L. Blumgart of Boston has summed it up "don't use it if your patient is not going to be dead of some other cause at the end of a year".*

A consideration of the literature and my own experiences have led me to prefer a forty per cent aqueous solution of methiodol as the contrast medium of choice. The particular substance used is that known as "Skiodan" in this country and "Abrodil" in Europe.† Skiodan is "Mono-iodo-methane of iodine in firm combination." The forty per cent solution is sterile and stable, casts a good shadow, is freely miscible with blood, and is easily injected, causing only mild discomfort. It is excreted by the kidneys, rendering the urine radio opaque and allowing good shadows of the urinary tract to be obtained by roentgenogram. It is almost entirely excreted inside of two hours. Its lack of general toxicity was determined in 1931 by Heathcote and Gardner[16] shortly after its introduction for use in intravenous urography. They used enormous doses intravenously in dogs, and found no damage resulting. The makers of Skiodan state that in the presence of serious bilateral impairment of renal function its injection is contraindicated. The universal adoption of this substance in intravenous urography and its very frequent performance without toxic effect attests to its safety from general toxicity.

In 1931 J. Schüller reported the results of two years of experience with arteriography[17]. He stated that he had performed this twenty-two times in man; first using seventeen to twenty-five per cent sodium iodide solution, which he abandoned as being too irritating; finally choosing twenty-two and one half per cent Abrodil, which he considered entirely satisfactory, giving good pictures, with little pain, and with no damage to the artery, as examined histologically. He added that, contrary to having any ill effect, the injection caused a subjective and objective hyperemia of the limb. Skiodan was also used by Frey and Zwerg[18] for the visualization of both arteries and veins in animals, and of veins alone in living people,—in strengths of twenty-five to forty per cent. They found no damage to the vessels and obtained good visualization. They considered this type of organic iodine compound superior to others.

A more detailed experimental and clinical examination of Skiodan was done by Pearse and Warren of the University of Rochester[19]. They filled emptied portions of arteries in dogs with a fifty per cent solution, and allowed it to act thus undiluted for one to five minutes before they removed the occluding clamps. Twenty-four to forty-eight hours later the vessels were free of thrombus, and when examined microscopically showed no damage to the intima. A factor of safety in their experiments is that they used only a forty per cent solution clinically, while they subjected the vessels of the dogs to a stronger solution, viz., fifty per cent. They made arteriograms of eight human cases; their reproduced pictures are excellent. In five of their patients amputation had previously been decided on and was done. In these, the arteries showed no fresh thrombosis or any other evidence of intimal damage. Wohlleben[20] also reports the use of a forty per cent solution of Skiodan in living patients, with excellent visualization of both veins and arteries, and with no deleterious effects.

I have personally used forty per cent Skiodan solution in the performance of twenty-four venographies and one arteriography, all in living patients. Good visualization was always obtained, even when used in vessels in which the blood flow was not interrupted. The venographies were performed in the course of experimental work on patients with varices, in many of which there was, of course, high-grade blood stasis, so that the Skiodan remained in long contact with the intima of the vessel. Many of these cases were operated on one to twenty-four hours later, and portions of the vein saved for histologic examination. In no case where Skiodan was used was there any thrombosis grossly or intimal damage microscopically. In one other case, in which another brand of iodide was used corresponding to Skiodan in its general use as a urographic agent, immediate phlebitis with total obliteration followed.

I have twice accidentally injected a small amount of the Skiodan outside the vein with but slight pain and no further reaction. I consider this an important attribute of Skiodan, as the similar escape of the other solution noted above resulted once in a severe inflammatory reaction.

VENOGRAPHY

The technic of venography varies according to whether one wishes to get merely anatomic data, or, in addition, information concerning the direction and rapidity of blood flow. If mere anatomic data are desired, the patient is placed recumbent on the x-ray table, the segment of limb to be examined is laid on a suitably sized x-ray plate, and is then isolated by one or two tourniquets. Fifteen to twenty cc. of forty per cent Skiodan is then rapidly injected into the vein, using an ordinary glass syringe and a needle of about 20 gauge. The x-ray exposure is started toward the end of the injection, so timed that the injection will be completed just before the end of the exposure. The total time of the injection is one minute or less. At

*Personal communication to the author.
†The Skiodan used was supplied through the kindness of the manufacturers, the Winthrop Chemical Co.

the end of the injection there is slight to moderate pain, which disappears as soon as the tourniquets are removed and the patient is allowed to move the limb, the Skiodan being washed away by the circulation. The clearest venograms are obtained in this way, as there is a minimum of dilution of the contrast material. (Fig. 2.) The additional visualization of the

FIG. 2. Venogram from a case of varicose ulcer of many years' duration. The patient had received sclerosing injections over a long period of time without healing of the ulcer. In spite of the absence of any visible varices, the venogram discloses many superficial veins connecting with the deep posterior tibial veins "D. V." through a valveless perforating vein "P. V." Note the presence of valves "V." in the deep veins. "U." is the ulcer area.

blood flow is also well accomplished by Skiodan. In this case no tourniquets are used, and the limb is placed in the horizontal or vertical position according to the purpose of the investigation. The x-ray film is placed on a stand or held behind the limb, and the injection and exposure made as noted above. Figure 3 illustrates the type of picture obtained, and the information to be derived from it. This patient was operated on eight years ago for large varices of the leg and the great saphenous vein removed. The uppermost level of the excision, however, was fifteen cm. below the termination of the saphenous. The patient presented large recurrences. With the patient standing the Skiodan was injected into the lower end of the stump of the saphenous vein. The venogram shows not only the large communications found between the saphenous and the varices below, but also that the direction of the blood flow is downward, indicating a loss of valve action and a high degree of severity of varicose dysfunction. In the obese patient, where the veins cannot be

FIG. 3. Venogram from a case of varicose veins recurring after low dissection of the great saphenous vein. See text. Note the needle in the stump of the saphenous at the upper end of the picture, and the rich anastomoses with collateral saphenous veins below. The flow is downward, that is—the reverse of normal.

well seen, venography will thus establish the result of the Trendelenburg test where the visual and palpable evidence is lacking. McPheeters and Rice[21] using lipiodol, and Barber and Orley[22] using Skiodan, have also demonstrated the value of venography in the study of varicose veins.

In the diagnosis of occlusion of the deep veins, venography is of distinct assistance. Figure 4 shows the venogram of a patient with thrombosis of the inferior vena cava of fifteen years' duration. Here, with the injecting needle well within the right femoral vein just above the saphenous opening, the entire flow is seen to reverse, returning through the saphenous opening, and then run upward through the dilated superficial epigastric vein to reach the internal mammary vein.

ARTERIOGRAPHY

The performance of arteriography is more difficult than venography. First, the artery to be studied is usually deeper placed, and secondly, practically total compression must be maintained proximal to the injecting needle, so that the rapid blood flow found here will not so dilute the fluid as to spoil its contrast.

A percutaneous injection may be made into the carotid, the brachial in the cubital fossa or the femoral in the femoral trigone. Most of the other vessels have to be reached by incision. The popliteal is so deeply placed compared with the femoral that the latter is used even when arteriograms of the lower part of the lower limb are desired. As in venography, the x-ray film and tube must be in position before the injection is made.

If incision is necessary, it may be carried out under novocain. If there is no x-ray machine

available in the operating room, the dissection may be carried out in the operating room and the injection made on the x-ray table. The needle is inserted into the vessel; the vessel is then compressed proximal to the puncture point and the injection and x-ray exposure are made as previously described. The arteries being valveless and the high back pressure being removed by the compression, the injected fluid quickly fills all the arteries present, through their anastomosing channels. (Fig. 5.) If the

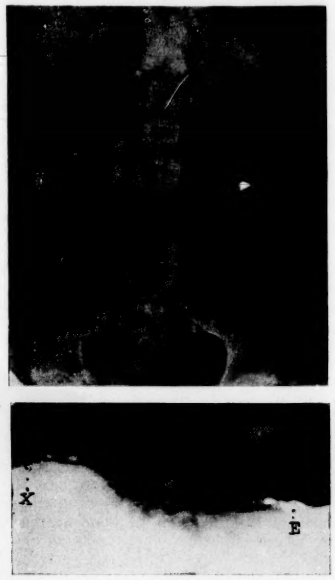

FIG. 4. Venogram from a case of thrombosis of the inferior vena cava of fourteen years' duration. See text. In the upper picture the patient is supine. The injecting needle is in the femoral vein too low to be seen. In the lower picture the patient is on his side. The injecting needle can be seen in the lower end of the dilated epigastric vein (position "E" in both pictures). The vein is seen to travel subcutaneously to the xiphoid "X" where it dips in to join the internal mammary vein. Note the absence of any iliac vein shadow.

x-ray exposure follows the injection by several seconds, the deep veins may be better visualized than the arteries. This is, indeed, a good purposeful way to visualize the deep veins.

In the performance of the injection through an incision, one should avoid actually stripping the artery clear from its surrounding structures thus minimizing the trauma to those structures, as well as to the artery and to its nerves.

The technique of arteriography is well described by dos Santos, Lamas and Caldas[12]. They made a small incision of three to four cm. through the skin and subcutaneous tissue. Then the depth of the wound is probed by the finger until the pulsation of the vessel is felt. The needle is passed along the finger to the pulsating vessel and punctures it. The only location where actual dissection of the vessel is imperative is in the axilla or arm, when the nerves of the brachial plexus are otherwise subject to injury. They use needles of .8 to 1 mm. in diameter (corresponding to our No. 20 or No. 19 gauge) and four to six cm. long. While one may use a larger needle with impunity in puncturing a vein, a hematoma is more likely to result if an artery is punctured with it. These authors make their injection with a pressure apparatus, but a simple glass syringe will suffice.

Saito and his co-workers[9] avoid the puncture of the main vessel by injecting into one of its branches as into the superior thyroid artery, when visualizing the carotid. I believe that this entails unnecessary dissection. A moment's pressure over the puncture point is sufficient to stop any bleeding if the needle has been a small one. As to the method of occluding the vessel while the injection is being made, I believe that simple digital compression or the application of a rubber tube tourniquet is efficient and safe. Lifting the vessel up on two threads which are then

FIG. 5. Arteriogram from a case of traumatic radial aneurism. The Skiodan was injected through the aneurism "A". Besides the arteries a large vein "V" is shown. This x-ray is reproduced through the courtesy of Dr. William Reid Morrison, who carried out the injection of Skiodan and subsequent successful excision of the aneurism.

pulled in opposite directions[17], or clamping the vessel[9], necessitates the stripping of the vessel and produces more trauma to it.

The amount of Skiodan used varies from ten cc. in the brachial artery to thirty cc. in the femoral. In cases of aneurisms, the size of the sac must be considered. If one injects too much, both the arteries and veins will be visualized; if too little, the terminal parts of the vessels in the limb will not be clearly shown.

Arteriography is perhaps more important

than venography in clinical work. I may cite a case from Schüller[17] to indicate its importance. A 53 year old man showed arteriosclerotic gangrene of the third, fourth and fifth toes of the right foot, with a line of demarcation across the middle of the dorsum of the foot. There was no pulsation in either the anterior or posterior tibial or the popliteal artery. The Moszkowicz test showed hyperemic reaction only to a level above the patella. Arteriography showed a fair anterior tibial and a poor position tibial artery, but a good peroneal artery. On the strength of the visualization of a good peroneal artery and against the evidence of absence of tibial pulsation, as well as the result of the Moszkowiez test, amputation was done at the mid-leg with good healing and recovery. Arteriography in cases of circulatory insufficiency thus gives the surgeon a chance to actually see the state of the vessels. Treatment does not have to be categorized by presumptive data, but can be individualized according to the arteriogram. It seems to the author that when the artery has to be bared, a peri-arterial sympathectomy or alcohol injection could be done, when indicated, at the same time.

In the study of aneurisms, arteriography is of great value. Dos Santos[12] gives six items to be determined by its use.

1. The variety of the aneurism.
2. Its exact relations.
3. The permeability of the sac.
4. The state of the collateral circulation.
5. The exact relation of arteries and veins in arteriovenous aneurisms.
6. The postoperative result.

One might well add that occasionally the diagnosis of aneurism of a peripheral artery is difficult to make, especially in the skull. Here arteriography is of great value. The method seems a good one to determine the degree of collateral circulation established in the treatment of aneurisms of peripheral arteries by progressive constriction by the metal band of Halsted[23].

Arteriography renders the localization of emboli exact. O. Loewe[24] reports a case of femoral embolism accurately localized by this means.

The site, extent, relations and vascularity of tumors may be determined by arteriography of the part. Saito et al[9] and Moniz et al[11] show excellent arteriograms of the head in verified cases of brain tumor with the tumor well outlined. Especially in the diagnosis of intracranial tumors, arteriography deserves a place among other procedures.

CONCLUSIONS

The x-ray visualization of veins and arteries (vasography) fills a need for more accurate data of these structures in experimental and clinical work.

The contrast medium of choice in this visualization should cast a clear shadow on the roentgenogram and should be free from pain on injection or local or general deleterious effect.

Among the various media tried, three seem to be deserving of future use. Two of these, however, Thorotrast and emulsified iodized oil, need further experimental and clinical data before they can be considered harmless,—Thorotrast because of its unknown ultimate toxicity due to its radioactivity, and the emulsified iodized oil because of the dangers from the intravascular injection of any oil.

Skiodan, in strengths up to forty per cent, seems ideal. It gives good clear vasograms, is easily injected without undue pain, and its lack of local or general toxicity has been well proved by animal and human experiments, and by the fact that a much larger dose than is used for vasography is universally used for intravenous urography.

The technic of venography is simple. The venogram gives exact information as to the size and shape and location of venous channels, and the direction of blood flow. It will indicate the presence or absence of functioning valves, of deep venous channels, of obliterated or recanalized varices.

Arteriography may be slightly more difficult than venography. In some cases, the artery is reached by percutaneous injection. In others, because it is more deeply placed, the artery may have to be reached by incision. The procedure is of importance in the diagnosis of the presence and degree of occluding disease; in the determination of the presence, variety, and relations of aneurisms, and the state of the collateral circulation; in the exact localization of an embolus; and in the diagnosis of the site, relations, and vascularity of tumors, particularly within the skull. When it is necessary to bare the artery by incision, a periarterial sympathectomy or alcohol injection can be done at the same time, where indicated.

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A DEVICE FOR MAKING RADIOGRAPHS OF THE GASTRO-INTESTINAL TRACT*

BY RICHARD DRESSER, M.D.,† AND FRANK SCHOLZ†

IT is now generally recognized by roentgenologists that a careful fluoroscopic examination is essential in every study of the gastro-intestinal tract. Many lesions can be shown only with the patient in very exact relation to the fluoroscopic screen, and in certain momentary phases of gastro-intestinal activity. Pressure must frequently be exerted in order to demonstrate some lesions, notably ulcers on the posterior gastric or duodenal wall. It is often impossible to obtain these relationships without visual control, and hence films made by the ordinary technique are of no value. It has been the wish of every fluoroscopist that he might record on a film the fleeting image which to him is diagnostic but which, without a radiograph, he cannot demonstrate to his colleagues. Moreover, in obese individuals the fluoroscopic image may be so faint that details cannot be satisfactorily made out. It then becomes highly important that numerous radiographs be made in proper phases of peristalsis, and in correct patient-film relationship.

A mechanism which will allow the recording of an image on a film within a second or less from the time it is seen on the fluoroscopic screen is of undoubted value. Such apparatus has been developed abroad (notably by Berg in Germany), but has attained little popularity in this country. This is perhaps due to the fact that most commercial apparatus of this type is expensive and cumbersome. Moreover, in certain makes there is too great a loss of time in making the change from the fluoroscopic to the radiographic setting.

It has been our aim to develop an apparatus of simple and inexpensive construction which, with a little ingenuity, can be attached to any modern radiographic-fluoroscopic unit.

The mechanism consists of a brass frame (figs. 1 & 2) which occupies the place of the usual fluoroscopic screen, and is attached to the fluoroscopic screen carriage by a wing nut at point A. This frame with its various accessories is approximately the same weight as the average fluoroscopic screen, so that no extra counterbalancing is necessary. The change from one to the other can be made in a few seconds. The frame is grooved at the top and bottom, and in these grooves slides a second smaller frame which accommodates a standard five by seven inch radiographic casette equipped with high speed double intensifying screens. The casette (B) is shown in figures 1 & 2 slipped half way into position. At the center of the large frame is attached a fluoroscopic screen (C) measuring six and one-half by eight and one-half inches which is large enough to visualize satisfactorily any given portion of the gastro-intestinal tract. The small frame carrying the casette may be slid from left to right, and vice versa by a handle (D). When the casette is in the left hand position it is completely protected from radiation by a piece of lead one-sixteenth inch in thickness. In the right hand position the casette lies directly behind the fluoroscopic screen in readiness to be exposed to the rays as soon as the foot switch is pressed. Moreover, when the casette is brought into the right hand position, a small trigger switch (E) is automatically tripped. This switch is connected through the flexible cable (F) to a double-pole solenoid. When the solenoid is closed, which is accomplished by the pressure of the casette on the trigger switch, two things are accomplished. First, the rheostat control in the radiographic unit is cut out, thus raising the voltage to any

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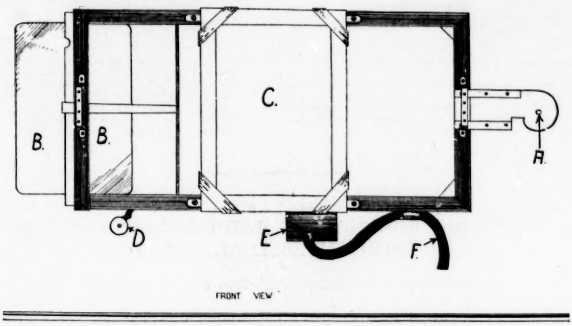


FIGURE 1

a. Point of attachment to fluoroscopic screen carriage
b. 5 x 7 casette
c. Fluoroscopic screen
d. Handle for shifting casette carriage
e. Trigger switch
f. Cable to solenoid

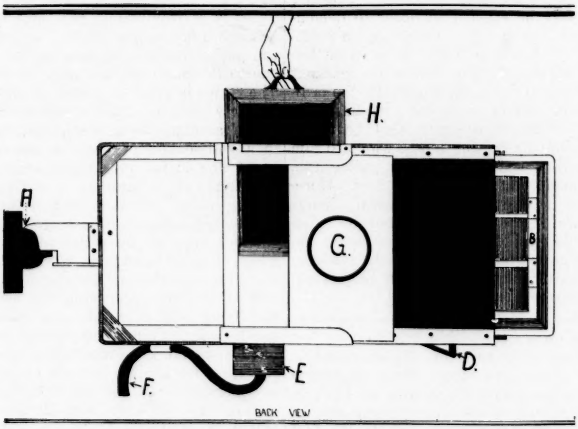


FIGURE 2

a. Point of attachment to fluoroscopic screen carriage
b. 5 x 7 casette
d. Handle for shifting casette carriage
e. Trigger switch
f. Cable to solenoid
g. Removable compression cone
h. Removable Potter-Bucky grid

given height as predetermined by the autotransformer setting. Secondly, an accessory filament control is thrown into circuit, thus raising the amperage to any predetermined height. It is necessary to use a circuit breaker for the large amount of current required in making fast radiographs of the gastro-intestinal tract. The circuit breaker supplied with any good auto-

matic timing device will prove satisfactory. The timer itself may be included in the circuit if desired, but with a little practice excellent radiographs can be made without a timer. A removable compression device, and fine grid Potter-Bucky diaphragm (figs. 2, G & H) are important accessories. We have constructed our own Potter-Bucky diaphragm, but should recommend the purchase of one of the small size Lysholm grids.

Figure 3 shows the switching mechanism attached to a fluoroscopic tilt table. It should be mentioned that the device works equally well in the vertical and horizontal positions. The procedure of operation is as follows: The motor starting switch of the x-ray machine is thrown in, or if the machine is of the valve tube type, the switch lighting the kenotrons is closed. The small frame designed to carry the casette, but without a casette in place, is slid to the right-hand position so that the trigger switch is tripped, which in turn closes the solenoid. The rheostat control is thereby thrown out of circuit, and the accessory filament control is thrown in. The accessory filament control is now set to give sixty milliamperes (or any other amount of current desired for making the radiograph), and the autotransformer is set for about ninety kilovolts peak. The frame is now moved to the left-hand position, thus releasing the trigger switch and solenoid. The machine is again adjusted by means of the rheostat and regular filament control to the fluoroscopic setting, let us say five milliamperes and eighty-five kilovolts peak. The five by seven casette is now slipped into the frame which is still in the left-hand position. The patient is placed in position for fluoroscopy and the lights are turned off. The fluoroscopic examination is carried out in the usual way. Whenever a radiograph is desired the frame carrying the casette is slid quickly to the right, and an exposure of a fraction of a second is made, using the same foot switch employed for fluoroscopy. The frame is then slid to the left, another casette is substituted for the one which has just been used for the exposure, and the fluoroscopy is continued. We have found the small Potter-Bucky grid of considerable value in the examination of obese patients. It may be used both for fluoroscopy and radiography. When compression is desired, the small cone designed for this purpose may be slipped quickly into place.

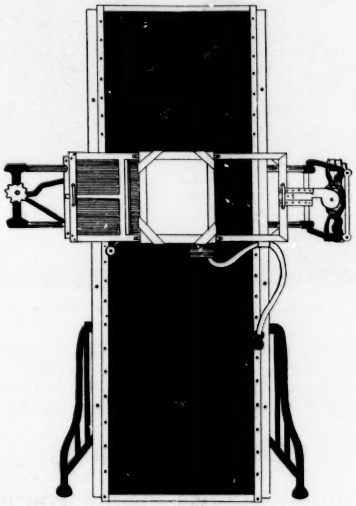
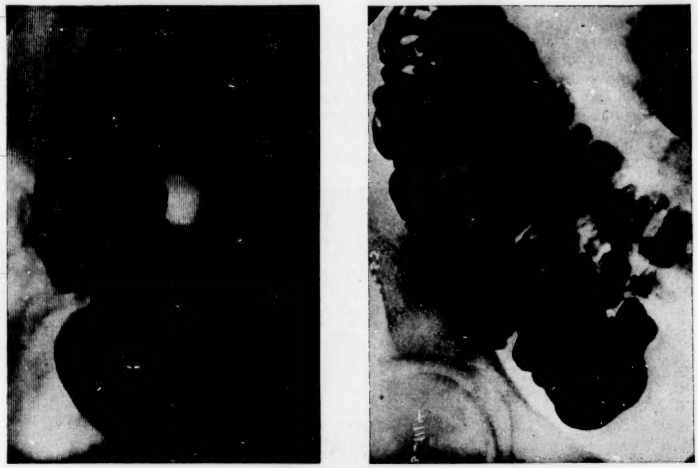


FIGURE 3
Switch mechanism attached to fluoroscopic tilt table

Although this apparatus has its greatest value

in the examination of the gastro-intestinal tract, a variety of uses at once suggests itself: for example, radiographs of the gall bladder in the upright position; localized views of the mediastinum in oblique positions; films of fractures during or immediately after fluoroscopic reduction, etc. Films of a normal stomach, and normal cecum are reproduced in figure 4 to show the size of the field included in the examination.



a. Normal stomach and duodenum b. Normal cecum

FIGURE 4

The cost of materials, construction, and installation of this apparatus including four casettes with double intensifying screens was approximately four hundred dollars.

MEDICAL PROGRESS

CARDIOVASCULAR REVIEW FOR 1932*

BY PAUL D. WHITE, M.D.†

INTRODUCTION

DURING the year 1932 many books and articles were published on cardiovascular disease, scattered through a wide range of aspects of the subject. The reviewer has selected 150 of these for mention because of their importance or special interest. The review is divided into convenient sections under the headings I. General, II. Anatomy and Physiology, III. Methods of Cardiovascular Examination, IV. Symptoms and Signs, V. The Incidence of Heart Disease, VI. Etiology, VII. Pathology, and VIII. Functional Disorders. Special interest has been exhibited as in previous years in the subjects of rheumatic heart disease, hypertension, and coronary disease.

*Prepared in March, 1933.

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GENERAL

Bramwell published during 1932 a small volume outlining the principles and practice of the diagnosis and treatment of heart disease following modern viewpoints. It is divided into seven parts: I. Introduction, II. Heart Failure, III. Disorders of the Cardiac Mechanism, IV. Structural Lesions, V. Cardiac Intoxications, VI. Blood Pressure, VII. Principles of Treatment and Prognosis.

The Criteria Committee of the Heart Committee of the New York Tuberculosis and Health Association has published a revised third edition of criteria for the classification and diagnosis of heart disease. The chief addition to this new edition consists of an appendix containing simple guides to the radiological and to the electrocardiographic diagnoses of cardiac

abnormalities, the former by G. Nemet and the latter by A. C. DeGraff. The nomenclature for cardiac diagnosis takes up, as previously: A. Etiological Diagnosis, B. Anatomical Diagnosis (Aorta and Pulmonary Artery, Coronary Arteries, Endocardium, Myocardium and Valves and Pericardium), C. Physiological Diagnosis, D. Functional Capacity, E. Possible Heart Disease, and F. Potential Heart Disease. This little book should prove helpful to those who are interested in heart disease but who are not familiar with present American viewpoints. One of the radiological terms which should be corrected for the sake of consistency is postero-anterior. This should read anteroposterior. If it is retained, then the other terms should be altered to be consistent, that is, right anterior oblique should be called left posterior oblique, and so on.

Bainton, J. H.; Levy, R. L.; De Graff, A. C., and Pardee, H. E. B.: Criteria for the Classification and Diagnosis of Heart Disease. N. Y. Tuberculosis and Health Association, New York, 1932. Third edition.

Bramwell, C.: Heart Disease. The Principles of Diagnosis and Treatment. Edward Arnold and Company, London, 1932. 244 pages.

ANATOMY AND PHYSIOLOGY

Rouvière has published an extensive and useful survey of the anatomy of the lymphatic circulation in man based on a critical review of the literature and on new injections and observations (a total of over 2,000).

Grollman has written a monograph in book form on the subject of the cardiac output of man in health and disease, giving a complete review of the literature and a bibliography of 483 titles, and recounting his own experiences with the acetylene gas method of determination of the cardiac output, which method he favors over all others, in spite of some limitations. In the first part of the book he discusses the early estimates of the cardiac output of man, the direct method for determining the output, indirect methods based on the Fick principle, methods based on the use of foreign gases (nitrogen, nitrous oxide, ethyl iodide, ethylene, and acetylene), and physical methods for determining the cardiac output (roentgen-ray, sphygmographic, and injection methods). In Part II, he describes and discusses the acetylene method. In Part III, he takes up the physiological variations of the cardiac output, emphasizing its constancy from day to day and the influence of posture, sleep, ingestion of food and fluid, menstrual cycle, psychic disturbances, temperature, muscular exercise, high altitude, and anoxemia. Under *Cardiac Index*, Grollman states that the cardiac output of normal individuals at rest is $2.2 \pm .3$ liters per minute per square meter of body surface, with average deviation from the mean of only 6.4 per cent. The maximum cardiac output observed on exercise was almost nine times the resting output; it was 37.3 liters. Part IV has to do with applications of cardiac output studies to pharmacology and therapeutics (including the effects of alcohol, caffeine, tobacco, carbon dioxide, digitalis, epinephrine, histamine, the nitrites, endocrines, massage, baths, and ultraviolet radiation). Part V deals with the clinical application of cardiac output studies in congenital heart disease, valvular disease, arrhythmias, pericardial disease, hypertension, blood diseases, hyperthyroidism, fever, and pregnancy. Finally, Part VI correlates cardiac output with other physiological functions like metabolism and velocity of blood flow.

Burridge has written an entertaining but abstruse discussion of the possible error of classic physiologic theories based on limited experimentation, particularly that on muscle in Ringer's solution. He says that not only must studies be made with varying environmental factors, but also stimulating factors must be used in widely different strengths, *e.g.*, strychnine in small doses stimulates and in large doses depresses the circulation. The vagus nerve decalcifies. The sympathetic nerve alters the "state of colloidal aggregation".

Skramlik has written a short volume giving a good summary of the anatomy and physiology of heart muscle based on comparative studies in the invertebrate and vertebrate.

Hill has recorded electrocardiographically the results of mechanical stimulation of the exposed vagus nerve and carotid sinus of man in a series of 20 cases operated on for malignant or tuberculous disease of the cervical glands. "Of thirteen cases under ether anesthesia, none showed any response to sinus stimulation, while one responded to vagal stimulation. Two cases under chloroform yielded responses to sinus stimulation, and one to vagal stimulation also. Of five cases under gas and oxygen, three gave responses to sinus or vagal stimulation, or to both. The response to sinus stimulation was usually moderate bradycardia, with or without diminution of the P-waves. A different response was elicited under chloroform, consisting of the appearing of ventricular extrasystoles. Responses to vagal stimulation were similar in nature, but were characterized by a longer latent period and longer after-effect."

Burridge, W.: Excitability. A Cardiac Study. Oxford Univ. Press, London, 1932. 208 pages.

Grollman, A.: The Cardiac Output of Man in Health and Disease. Charles C. Thomas, Springfield, Ill., 1932. 325 pages.

Hill, I. G. W.: Stimulation of the vagus nerve and carotid sinus in man. Quart. J. Exper. Physiol. 22:79, 1932.

Rouvière, H.: Anatomie des lymphatiques de l'homme. Paris: Masson et Cie., 1932.

Skramlik, E. von: Herzmuskel und Extrareize. Verlag von Gustav Fischer, Jena, 1932. 224 pages.

METHODS OF CARDIOVASCULAR EXAMINATION

Auscultation.—Fineberg and Steuer have reported a follow-up study that they have made of 100 children with uncomplicated apical systolic murmurs. The average duration of the follow-up study was six years, the maximum in any case being 15 years. "Of all the patients, 30 per cent developed serious complications (mitral stenosis, aortic insufficiency, or both). Of those giving a history of rheumatic fever or chorea 50 per cent developed serious cardiac complications. Among those showing clinical enlargement at the first examination 37 per cent developed serious cardiac manifestations. Of those showing enlargement by orthodiagram 40 per cent developed serious cardiac manifestations. . . . Only 8 per cent of the patients showed complete disappearance of the murmur. . . . The electrocardiogram seemed to be of no value in estimating the prognosis."

Hiestand and Morris have reported finding that the systolic murmur of aortic stenosis was transmitted to the abdominal aorta in 9 out of 11 cases, while the systolic murmur of luetic aortic disease with aortic regurgitation was similarly transmitted in all of five cases.

Fineberg, M. H., and Steuer, L. G.: Apical systolic murmurs in children. Am. Heart J. 7:553, 1932.
Hiestand, R. F., and Morris, R. S.: Note on the transmission of aortic systolic murmurs to the abdominal aorta. Am. Heart J. 8:249, 1932.

Blood and Urine Studies.—Lichtman and Gross have found in a study of 5,233 consecutive blood cultures in a general hospital, nonhemolytic streptococci (alpha and gamma) on an average of six plus per cent (varying from four to 15.5 per cent) in nine different diseases: acute rheumatic fever with polyarthritis (8 per cent), chronic rheumatic cardiovalvular disease (5 per cent), rheumatoid arthritis (4 per cent), aplastic anemia (15.5 per cent), pernicious anemia (5 per cent), leukemia (7 per cent), colitis (10 per cent), meningococcus meningitis (4 per cent), and pyelitis and pyelonephritis (7 per cent).

Reith and Squier have reported an important study of blood cultures of 293 relatively healthy persons. Positive blood cultures for streptococci, diplococci, diphtheroids, *M. catarrhalis*, colon bacilli, and obligatory anaerobic rods were obtained from 53, or 27 per cent, of 194 persons who had chronic focal infections, while such cultures were obtained from only 12 per cent of 99 persons who had no evidence of any infections.

Lichtman, S. S., and Gross, L.: Streptococci in blood in rheumatic fever, rheumatoid arthritis and other diseases; based on study of five thousand two hundred and thirty-three consecutive blood cultures. Arch. Int. Med. 49:1078, 1932.
Reith, A. F., and Squier, T. L.: Blood cultures of apparently healthy persons. J. Infect. Dis. 51:336, 1932.

Blood Pressure Estimation.—Dameshek and Loman have compared the intra-arterial brachial blood pressure as determined directly by arterial puncture, with that determined by the usual indirect methods in 150 individuals with normal or sclerosed blood vessels. They found the indirect methods to be reasonably accurate even when there was marked arteriosclerosis. Errors at most were not more than 10 to 20 mm. of mercury, and such errors were due to high pulse pressure rather than to the hardness of the wall of the blood vessels.

Vaquez and Lajoie have revived the idea of the clinical significance of the average dynamic blood pressure first stated by Potain forty years earlier. This average pressure the authors define as "that in which there exists a constant pressure régime, that would assure during a certain interval the same flow of blood in the vessel, as is furnished by the régime of the variable pressure which reigns normally in the artery." This average pressure, the authors believe, may be easily determined by routine methods, since they think it is recorded by the maximal oscillations of the oscillometric sphygmomanometer during decompression. It is a little above the diastolic pressure level; in 200 normal individuals the authors found it to lie between 80 and 100 mm. mercury, and to be a physiological constant not influenced by exercise, part of body, etc.

Plesch has published a study dealing with the effective blood pressure and the rôle of blood vessel functions in relation to the work of and the strain on the heart. In the first of the two papers, he agrees with the conception put forth by the French school (beginning with Potain, including Pachon later, and most recently represented by Vaquez) that the most important blood pressure measurement is not that of either the systolic level, the diastolic level, or the pulse pressure, but the "effective pressure" which is the pressure which applied constantly would move the same blood mass through the arteries that is moved in any given case by the pressure which varies from maximum to minimum. In discussing the oscillations of pressure, Plesch states that the maximal swing is the sum of two components: (1) the minimum pressure, i.e., the lowest pressure which exists in the vascular system during a given oscillation, and (2) the tension of the wall. Since the tension and elasticity of the arterial wall vary independently of the blood pressure, Plesch denies the validity of Vaquez's assertion that the maximal oscillations of blood pressure, as determined for example by Pachon's oscillometer, represent the effective pressure. Plesch himself has determined the effective pressure in a given case by applying pressure by a blood-pressure cuff on the upper arm just below the systolic level and finding out what external pressure is needed, in an air chamber surrounding the lower arm and hand, to collapse the distended veins (seen through a window), by driving the blood back

into the arteries through the capillaries. The effective pressure determined in this way is in the average person only between 10 and 20 millimeters above the minimum pressure. Plesch concludes that the variations of the effective pressure are satisfactorily indicated by the parallel variations of the easily estimated minimum pressure and that, therefore, we can draw sufficiently accurate clinical conclusions from the level and variations of the minimum pressure without determining the effective pressure. However, the reviewer notes that in Figure 6, even Plesch himself admits that the effective pressure may vary from just above the minimum pressure to half way between the maximum and minimum pressures.

In the second communication on blood vessel function, Plesch discusses first the work and strain on the heart. The product of the greatest stroke volume and the highest pulse frequency must be greater than the minute volume. "Volume insufficiency" of the heart gives rise to dilatation of the heart, which is constantly accompanied by hypertrophy, and this produces "eccentric hypertrophy." "Force insufficiency" of the heart gives rise to hypertrophy without dilatation, or "concentric hypertrophy." Eccentric hypertrophy is characteristically found with valvular defects and concentric hypertrophy with hypertension. A third type of ventricular insufficiency is inability or failure of the heart to meet the demands on it, i.e., heart weakness. Plesch believes the auricular contraction is important, failure of the auricular musculature forcing after it a volume insufficiency.

For every accurate cardiac prognosis, the author states that an exact vascular diagnosis is essential. With respect to blood pressure the maximal or systolic is of little or no moment; only the minimum and pulse pressures are of diagnostic significance. The pressure amplitude is the volume fluctuation of the artery during a pulsation multiplied by the elasticity constant of the arterial system. The minimum pressure is a measure of the permeability of the capillaries and the pressure amplitude is a measure of the elasticity constant of the arterial system. For the work of the heart the effective (and minimum) pressure is the important value. A higher minimum pressure means increased heart work, whereas a higher maximum pressure signifies a stiffer vascular system. A work hypertrophy of the heart comes not with demand of the maximum but rather of the minimum pressure. The "volume needs" of the circulation depend upon metabolism; the "force need" is dependent on four factors: (1) minute volume, (2) precapillary resistance, (3) pulse frequency, and (4) elasticity constant. The accommodating pressure changes in the vascular system are independent of the heart and alone dependent on the state of the vascular system. Arterial activity—elasticity—is essential to life. Arterial calcification is not the disease itself but a protection reaction.

Finally, in the clinic it is possible for us as yet to draw only qualitative conclusions as to the significance of the minimum (or effective) pressure and amplitude of the pulse, since of four factors behind these two readings only *one* is known:

Minimum pressure = stroke volume × *frequency* × capillary resistance; and amplitude = stroke volume × elasticity constant.

Evans has written a good review of venous pressure in man, and recommends the direct method of estimation as relatively simple and consistently reliable. A personal experience of 175 observations is cited.

Dameshek, W., and Loman, J.: Direct intra-arterial blood-pressure readings in man. Am. J. Physiol. 101:140, 1932.
Evans, W.: Venous pressure. New Eng. J. Med. 207:934, 1932.
Plesch, J.: Funktionelle Gefässdiagnostik. I. Mitteilung. Der effektive Blutdruck. Ztschr. f. klin. Med. 121:628, 1932. Funktionelle Gefässdiagnostik. II. Mitteilung. Die funktionelle Gefässdiagnostik als Vorbedingung für die Prognose des Herzens. Ztschr. f. klin. Med. 121:640, 1932.
Vaquez, H., and Lajoie, R. J.: The Physiological and Clinical Study of the Average Dynamic Blood Pressure (Pression Moyenne). Libman Anniversary Volumes. 3:1163, 1932.

Electrocardiography.—Boden has published an excellent small volume on clinical electrocardiography for German students and practicing physicians. It is arranged in a systematic and readable form of fourteen lectures, beginning with theoretical considerations and concluding with practical applications in clinical medicine. The illustrations, 91 in number, are unusually clear and instructive.

Edeiken and Wolferth discovered no significant Q-3 waves in the electrocardiograms of 709 apparently normal college students. "Among 117 college athletes, the only significant Q-3 wave occurred in an individual with rheumatic heart disease. A significant Q-3 wave was found in approximately 6 per cent of 500 hospital ward and clinic patients with cardiovascular disease. . . . Hypertension, arteriosclerosis, and syphilis were regarded as the etiological factors of the heart disease in the majority of cases, but significant Q-3 waves were also seen in cases of rheumatic and thyrotoxic heart disease. In 1900 unselected electrocardiograms taken from the files of the Cardiographic Laboratory, including ward, clinic, and private patients of all ages, there were 78 (4.1 per cent) significant Q-3 waves. Of the 78 individuals exhibiting the significant Q-3 waves, 63 were classified as having heart disease, 7 were placed in a doubtful group, 5 were considered negative, and 3 were not classified because of inadequate records. Thirty-one, or 26.7 per cent, of 116 cases of the anginal syndrome showed a significant Q-3 wave." "Of a total of 149 electrocardiograms with significant Q-3 waves, 68 were otherwise normal, 64 showed T-wave changes, and 17 showed other abnormalities. This sign, therefore, may constitute the first electrocardio-

graphic change to invite attention to the possibility of cardiac damage. Twenty-five pregnant women in the ninth month were electrocardiographed, and 3 were found to show significant Q-3 waves. In 2 of these who were reëxamined several months after delivery, the Q-3 wave had vanished". The authors conclude that "available evidence indicates that the conditions chiefly responsible for deep Q-3 waves are either (1) a lesion of the septum which interferes with the spread of the excitatory process, or (2) deviation of the septum from its usual position with reference to Lead III of the electrocardiogram."

Holzmann and Scherf have discussed electrocardiograms with shortened atrioventricular distance and positive P deflections. In the first part of their paper, they reported two new cases of the electrocardiographic syndrome described by Wolff, Parkinson, and White consisting of positive P waves in all three leads, a shortened P-R interval (0.1 second or less), widened QRS complexes, and occasional attacks of supraventricular paroxysmal tachycardia. On the basis of the analysis of the curves, the authors reject the previous explanations of these tracings. Neither an unusual vagal effect nor a-v nodal rhythm seems likely, but rather an abnormal conduction path between auricles and ventricles outside of the a-v node. Less probable is the theory that the auricular contraction mechanically sets off a ventricular contraction by stimulating an abnormally irritable focus or center in the ventricles. The fact that in 15 of the 17 cases described so far there is in addition to the electrocardiographic changes auricular paroxysmal tachycardia points to a definite relationship the explanation of which is today still obscure. It is the present belief of the reviewer that the idea of an unusual congenital sidetrack for conduction from auricle to ventricle is a reasonable as well as an ingenious explanation of this unusual rhythm (bringing to mind the extra bundle once described by Kent, 1892).

In the second part of their paper the authors describe curves with positive P waves, shortened P-R intervals, and *normal* ventricular complexes. In these cases the probability is presented that the origin of the heart beat lies either in the a-v node or in the lower end of the sinus node. However a certain explanation is not possible as yet in the light of our present knowledge.

Kountz and Hammouda have found that "perfusion of coronary arteries of the dog with asphyxial blood produces changes in the electrocardiogram similar to but more marked than those produced by clamping the coronary arteries. These changes in the electrocardiogram are found to be comparable to those observed in coronary diseases in the human heart."

Speckman and Rich have presented evidence confirming the importance of low voltage in the electrocardiogram as a sign of heart trouble. Forty-one out of 50 cases gave clinical evidence of heart disease.

Turner has analyzed the records of 164 patients who showed low voltage in their electrocardiograms. All but 51 showed evident heart disease, mostly with congestive failure, and the low voltage was a serious prognostic sign. The 51 cases without manifest heart disease had variable pathological conditions, such as pneumonia.

Boden, E.: Elektrokardiographie für die ärztliche Praxis. Verlag von Theodor Steinkopff, Dresden and Leipzig, 1932.
Edeiken, J., and Wolferth, C. C.: The incidence and significance of the deep Q-wave in lead III of the electrocardiogram. Am. Heart J. 7:695, 1932.
Holzmann, M. and Scherf, D.: Über Elektrokardiogramme mit verkürzter Vorhof-Kammer-Distanz und positiven P-Zacken. Ztschr. f. klin. Med. 121:404, 1932.
Kountz, W. B., and Hammouda, M.: Effect of asphyxia and of anoxemia on the electrocardiogram. Am. Heart J. 8:259, 1932.
Speckman, R. N., and Rich, M. L.: An analysis of fifty heart cases showing low voltage. J. Lab. & Clin. Med. 17:165, 1931.
Turner, K. B.: Low voltage in electrocardiogram; occurrence and clinical significance. Arch. Int. Med. 50:380, 1932.

Roentgenology.—Padilla, Cossio, and Berconsky have reported a study in 4 patients of the position of the superior vena cava in the roentgen-ray shadow of the great vessels, by the introduction of a catheter through the veins into the right auricle. Three of the cases died with the catheter still in situ in the superior vena cava. Roentgen-ray study and postmortem examination proved that the right border of the shadow of the great vessels is made up of the superior vena cava even when there is a pulsating convexity to the right just above the heart. The aorta lies to the left of the superior vena cava normally and also in abnormal instances when it bulges to the right; in the latter case it displaces the vena cava also to the right.

White and Camp have reported a study of comparative orthodiagraphic and teleroentgenographic measurements of the heart and thorax in a series of 22 individuals, 10 normal and 12 with abnormalities of heart, aorta, or pericardium. The transverse diameter of the heart averaged about 1 cm. greater by teleroentgenogram than by orthodiagram and the internal diameter of the thorax 2.5 to 2.75 cm. greater. The cardiothoracic ratio was essentially the same by both methods. The cardiac area averaged 15 to 25 per cent greater by teleroentgenogram than by orthodiagram. The authors concluded that, "in giving roentgen measurements of cardiac and intrathoracic diameters and of cardiac area it is essential to state whether these measurements are made by orthodiagram or by teleroentgenogram. The difference between the results of the two methods is great enough to render direct comparison misleading."

Pezzi has written a review of his original observations of the radioscopic sign of the "hilum dance," which consists of the rapid expansion

and equally rapid collapse of the lung hilum mass. He states that in the great majority of cases it is pathognomonic of insufficiency of the pulmonic valves but may occur also in rare cases of patency of the ductus arteriosus when the reflux of blood is from pulmonary artery into aorta and not vice versa, and, finally, in rare instances of pulmonary hypertension with very slow pulse resulting in much accentuated pulse pressure without pulmonary valve regurgitation. It accompanies primary pulmonary arteriosclerosis only when there is also pulmonary regurgitation, though the hilum shadows are denser in such cases and so the dance is more evident. The visual impression of the hilum dance on the screen is analogous to that seen in the peripheral arteries when there is marked aortic insufficiency.

Desjardins has published an excellent review of the action of roentgen rays and radium on the heart and lungs.

Desjardins, A. U.: Action of roentgen rays and radium on the heart and lungs. Am. J. Roentgenol. 27:149 and 477, 1932.

Padilla, T., Cossio, P., and Berconsky, I.: Catheterization of right heart; rôle of superior vena cava in projection of right outline of supracardiac shadow of great vessels of heart in roentgen picture. Semana méd. 2:391, 1932.

Pezzi, C.: The Radioscopic Sign of the "Hilum Dance"; Its Significance. Libman Anniversary Volumes. 3:931, 1932.

White, P. D., and Camp, P. D.: A comparison of orthodiagraphic and teleroentgenographic measurements of the heart and thorax. Ann. Int. Med. 6:469, 1932.

SYMPTOMS AND SIGNS

Dyspnea.—McGinn and White have published a follow-up report on a series of 250 cases of cardiac asthma to the deaths of 230 of them, along with an analysis of an additional group of 22 cases. "Patients presenting this symptom of organic heart disease are most frequently males over 50 years of age with hypertensive or coronary heart disease. Although exceptions are not uncommon, the average expectancy of life has been found to be little more than 2.0 years, one out of four patients dying within six months. The better the treatment, the longer the life. Rarely a patient may become free of attacks. The prognosis is much more serious when cardiovascular syphilis is the underlying factor or when cardiac asthma is associated with congestive failure, aortic regurgitation, or auricular fibrillation. The presence of pulsus alternans, gallop rhythm, or very severe long attacks likewise make the outlook dubious. Chronic passive congestion and left ventricular hypertrophy were the outstanding findings in 15 postmortem examinations. The most effective treatment of acute attacks of cardiac asthma has consisted of the hypodermic injection of morphine and the assumption of the upright position; these measures have generally been successful. Venesection has been rarely required, but it should be carried out in severe attacks. Diuretics whether or not there have been signs of congestive heart failure have been beneficially added to the usual rest and digitalization prescribed for these patients. The establishment and maintenance of an adequate digitalis effect are of the greatest value in most cases for the prevention of cardiac asthma and the prolongation of life." A few cases of "pure" mitral stenosis have been encountered in this study of cardiac asthma in which left ventricular strain and failure have not been the cause of the attacks but rather acute engorgement of the lung circulation, during a tachycardia, doubtless due to the inability of the blood pumped by the right ventricle to pass rapidly enough from the lungs through the narrowed obstructing mitral orifice.

McGinn, S. and White, P. D.: A follow-up report on the clinical study of two hundred and fifty cases of cardiac asthma and a survey of an additional group of twenty-two new cases. New Eng. J. Med. 207:1069, 1932.

Pain.— Capps has assembled and published in monograph form his interesting and valuable observations on pain in the pleura, pericardium, and peritoneum in man. He agrees with Mackenzie that dry pericarditis is usually a painless disease. "The presence of pain with pericarditis can be adequately explained by three complications as follows: *First,* a large effusion exerting extreme tension on the pericardial sac. This may give rise to a dull ache or feeling of oppression over the heart. *Secondly,* a myocardial involvement due to embarrassment of the coronary circulation. The pain is that of angina pectoris. *Thirdly,* a pleuro-pericarditis which may be confined to the mediastinal region or may extend to the diaphragmatic pleura. The pain in these cases may be localized over the heart or be referred to the neck (if the diaphragmatic surface of the pleuro-pericardium is involved) or abdomen. Of especial importance in their recognition is the exciting factor of movement of the thorax and diaphragm from deep inspiration and cough."

Capps, J. A.: Pain in the Pleura, Pericardium, and Peritoneum. A Clinical Study. The Macmillan Company, 1932.

Edema.—Barker has made experimental observations on the relation of sodium and potassium to body fluid balance in cases of cardiac and nephrotic edema. He found "that twelve of sixteen patients lost their edema when given potassium chloride, provided they were placed on a full general diet with an acid ash excess in which a low ratio of sodium to potassium was maintained. Some cases responded dramatically and others less. No cause for the success or failure of this regimen has been found. No ill effects from the procedure have been noted in cases followed as long as a year and a half. No conclusions can be drawn from these observations" according to the author, except that

this procedure is worthy of trial in the case of patients who fail to respond to the usual measures.

Darrow, Hopper, and Cary have shown that "dogs rendered edematous by plasmapheresis show a type of edema closely analogous to that of cases of nephrosis, hydropigenous nephritis, nutritional edema and cachectic states. Low plasma protein should not be considered a cause of permanent renal damage. . . . There seemed to be a critical concentration of 3 to 3.5 per cent total plasma protein at which edema appeared. The critical concentration of 1.5 per cent. albumin seems to determine the production of edema more regularly than the total protein concentration." (Edema comes with total protein osmotic pressure below 12 mm. mercury.)

Lian defines acute pulmonary edema as an attack of suffocation accompanied by the expectoration of more or less mucus, often reddish and always strongly albuminous, caused by a sudden inundation of the pulmonary alveoli by an abundant transudation of serous fluid. His etiologic, pathogenic, clinical, and therapeutic studies covered a period of twenty years. In the etiology are considered diseases of the aorta, arterial hypertension, and nephritis, and, also other factors, the mitral valvular cardiopathies, acute infectious diseases, intoxications, nervous diseases, cerebral embolism and thrombosis, and complications of thoracentesis and abdominal paracentesis. After a discussion of the pathogenesis, Lian concludes that pulmonary edema is due to the summation of two mechanical factors: insufficiency of the left ventricle and vasomotor nervous disturbance. Among the clinical forms he discusses the bronchoplegic, the attenuated and the localized forms, and the forms caused by mitral stenosis, acute infectious diseases and war gas. Diagnosis is not difficult but it is important to differentiate cardiac pseudoasthma and acute pulmonary edema. Prognosis depends on the amount of expectoration and on the resistance of the patient's cardiovascular system. The author bases prescription of treatment on the two factors prominent in acute pulmonary edema: the insufficiency of the left ventricle and the vasomotor disturbances.

Barker, M. H.: Edema as influenced by a low ratio of sodium to potassium intake; clinical observations. J. A. M. A. 98:2192, 1932.

Darrow, D. C., Hopper, E. B., and Cary, M. K.: Plasmapheresis edema. I. The relation of reduction of serum proteins to edema, and the pathological anatomy accompanying plasmapheresis. J. Clin. Investigation. 11:683, 1932.

Lian, C.: Acute Pulmonary Edema. Arch. méd.-chir. de l'app. respir. 6:345, 1931.

Other Signs.—Dressler has written a review of the pulsatory movements of the thoracic wall in normal persons and in those with heart disease, including his own studies, made with the help of graphic records, of a large variety of pathological conditions. Among other observations, he emphasizes the need of not confusing cardiac enlargement (with tricuspid insufficiency) with pericardial adhesions and subjecting the patient to a Brauer's operation simply because it is observed that there is a systolic depression of the precordial region.

Padilla, Cossio, and del Castillo have discussed the sign of generalized thoracic pulsation consisting of a systolic elevation of the left half of the anterior thoracic wall and a simultaneous depression of the right half. This generalized thoracic pulsation is caused by the systolic dextrotorsion of the heart wedged in between the vertebral column and the anterior chest wall, this wedging process resulting either from retrocardiac aortic aneurysm or thoracic tumor or from the enlargement of the heart alone.

Kellogg and White have reported an analysis they have made of 328 cases showing precordial tenderness among 3770 consultation cases with cardiac symptoms or signs. Only 79 were male, while 249 were female. The majority were over forty years old. The authors conclude that "precordial tenderness may occur in an individual with a hypersensitive nervous system whether or not there is serious heart disease. In the present series it was more often found when there was a combination of heart disease and nervousness than with either condition alone. The factor of nervous irritability and fatigue is certainly of greater importance in the production of the sign than is organic cardiovascular disease itself, for in cases of very severe acute and fatal coronary thrombosis there may be no tenderness whatsoever, and in many nervous individuals with perfectly normal hearts there is well-marked precordial tenderness."

Ottenberg has discussed jaundice in heart failure and has pointed to several causative "factors, no one of which is alone responsible for producing it. A combination of two or more are necessary. They are as follows: (1) *Increased production of bilirubin* in all the tissues where it is produced, but especially in the lungs and spleen and perhaps in the liver. This is probably due to the slowed circulation and the resulting prolonged anoxemia of the red blood cells leading to their destruction. (2) *Profound depression of the excretory function of the intact liver cells* for bilirubin as the direct result of lack of oxygen. (3) *Actual atrophy of liver cells* at the centers of the lobules. This is now believed to be also a secondary result of anoxemia rather than of mechanical pressure. . . . (4) *Slowing of the circulation* so that only a small fraction of the usual amount of blood passes through the liver to be cleared of its bilirubin." The failure of edematous parts of the body to become jaundiced in some cases of heart failure which show both edema in part of the body and jaundice in the rest is probably due to the fact that bilirubin is almost wholly insoluble in edema fluid because of its low protein content.

Dressler, W.: Die pulsatorischen Bewegungen der Brustwand bei gesunden und krankem Herzen. Wien. klin. Wchnschr. 45:387, 1932.
Kellogg, F., and White, P. D.: The clinical significance of precordial tenderness—The relationship of such tenderness to pain. New Eng. J. Med. 206:659, 1932.
Ottenberg, R.: Jaundice in Heart Failure. Libman Anniversary Volumes. 3:917, 1932.
Padilla, T., Cossio, P., and Castillo, E. B. del: Generalized Thoracic Pulsation. Semana méd. 1:769, 1932.

THE INCIDENCE OF HEART DISEASE

Schwab and Schulze have reported a study of the incidence of heart disease among 10,188 new patients (4,252 white and 5,936 Negro patients) seen in the Medical Division of the Dispensary of the John Sealy Hospital, Galveston, Texas, during the past seven and one-half years. One thousand six hundred and sixty cases of organic heart disease were found in this group, including 488 white patients and 1172 Negroes, which gives a relative incidence of 11.5 per cent for whites and 19.7 per cent for Negroes. The average age of the Negro cardiac patients was 46.6 years and of the whites 56.3 years. Hypertensive cardiovascular disease was found to be the commonest type in the Negro, making up 12.5 per cent of the dispensary Negro patients or 63.5 per cent of the Negro cardiacs. It occurred nearly three times oftener than in the whites and was 1½ times more common in the female than in the male. Cardiovascular syphilis occurred in 15 per cent of the Negro cardiac patients and was four times more frequently found in the Negroes in the clinic than in the whites. Coronary disease was found in 14 per cent of the Negro cardiac patients and both relatively and absolutely was considerably more common among the whites. Angina pectoris was found in only 11 of the white patients and in none of the Negroes. Rheumatic heart disease and thyrotoxic heart involvement were apparently rarely found among the Negroes.

Schwab, E. H., and Schulze, V. E.: Heart Disease in the American Negro of the South. Am. Heart. J. 7:710, 1932.

ETIOLOGY

Congenital Heart Disease.—Abbott has presented a complete survey of the relative incidence and clinical significance of a congenitally bicuspid aortic valve. The combined statistics of Abbott and of Lewis and Grant show 147 cases of congenitally bicuspid aortic valve associated with other anomalies and 169 "primary" (uncomplicated) cases. Three important clinical complications may occur in such cases: (1) Sclerosis resulting in calcification, deformity, and chronic valvular disease, (2) subacute infective involvement, and (3) dissecting aneurysm with subsequent spontaneous rupture of the ascending aorta. Of five case reports presented by Abbott in this paper, three showed congenitally bicuspid aortic valves and two an inflammatory fusion.

Willer and Beck have reported the detailed macroscopic and microscopic findings in two hearts showing congenital stenosis of the ascending aorta with atresia of the aortic ostium; these specimens were obtained from male infants who died three and four days after birth, respectively. In each case, the right ventricle, pulmonary artery, and patent ductus arteriosus were much enlarged, while the thick-walled left ventricle showed a very small cavity and the coronary artery mouths were small. Microscopic examination indicated that fetal endocarditis had been the cause of the aortic valve lesions.

White and Boyes have reported the unique case of a young woman, aged twenty-one, with the tetralogy of Fallot complicated by congenital pulmonary regurgitation and with death resulting from subacute bacterial (*Streptococcus viridans*) endocarditis and endarteritis involving the tricuspid valve and the pulmonary artery.

Abbott, M. E.: On the Relative Incidence and Clinical Significance of a Congenitally Bicuspid Aortic Valve. Libman Anniversary Volumes. F. 1, 1932.
White, P. D., and Boyes, J. H.: Subacute bacterial (streptococcus viridans) endocarditis and endarteritis involving the tricuspid valve and the pulmonary artery in a unique case of the Tetralogy of Fallot complicated by congenital pulmonary regurgitation. Am. Heart J. 7:802, 1932.
Willer, H., and Beck, L.: Über angeborene Stenosen der Aorta ascendens mit Atresie des Aortenostiums. Zugleich ein Beitrag zur Frage der fetalen Endokarditis. Ztschr. f. Kreislaufforsch. 24:633, 1932.

Rheumatic Heart Disease.—Coburn and Pauli have made the following conclusions after studies of the relationship of *Streptococcus hemolyticus* to the rheumatic process: "Certain factors of climate are favorable to streptococcus respiratory diseases. In those tropical environments where hemolytic streptococcus is unusual in the throat flora, scarlet fever is unknown and rheumatic fever rare. In New York City, however, following epidemic waves of pharyngitis with hemolytic streptococcus the incidence of rheumatic fever rises precipitously. The correlation between the geographical distribution of hemolytic streptococcus and rheumatic fever is a definite one.

"Furthermore, in New York City during the seasons of the year in which hemolytic streptococcus is seldom recovered from the pharynx, acute attacks of rheumatism are unusual. Corresponding to the seasonal rise in hemolytic streptococcus infections, the curve of incidence of acute rheumatism shows a similar form.

"Among the children of wealthy patients, enjoying great protection, hemolytic streptococcus has been recovered infrequently from the throat, and rheumatism has not been encountered during this study. Among the poor under observation in New York City, however, the organism is found frequently in the pharyngeal flora, and rheumatic fever is common. The findings suggest that poverty and unhygienic living conditions favor both the activity of hemolytic streptococcus in the throat and the incidence of rheumatic fever.

"Moreover, localized outbreaks of rheumatism have been observed frequently following epidemics of 'sore throat'. Bacteriological

studies of these upper respiratory infections demonstrate a close relationship between the advent of hemolytic streptococcus in the throat flora and the outbreak of rheumatic fever in susceptible individuals. . . .

"Hemolytic streptococcus in most instances appeared in the pharynx from 1 to 5 weeks before the onset of the rheumatic attack. These organisms have been investigated with the usual types of bacteriological tests and, in addition, have been classified serologically according to Lancefield's technique. The results have demonstrated that the organisms were not of a single type, but fell into six antigenic groups. The majority of the freshly isolated strains tested were strong toxin producers. The organisms producing the strongest toxin were cultures from the patients who developed extremely intense rheumatism. About 70 per cent of these toxins were neutralized by a monovalent streptococcus antiserum. . . .

"Precipitin tests indicate that at the time of appearance of the rheumatic attack, individuals develop, in their blood, precipitins to the protein fractions of hemolytic streptococcus. That these precipitins may not be entirely specific is recognized from their cross-reactions with antigens of chemically related organisms." Also, "there occurs in each instance a rise in the antistreptolysin titer of the patient's serum. This titer is much higher than that observed in normal subjects or in patients with bacterial infection other than hemolytic streptococcus."

Schwarz has described a rare case of rheumatic fever in a male infant, aged seventeen months; there was pain in the right foot at first, then fever. No heart murmurs were found. The hemoglobin was 50 to 55 per cent, the red cell count 3,770,000, the white count 22,650. Roentgen-ray examination of the chest was negative. Postmortem examination showed the lungs and abdomen negative except for moderately severe bronchitis. The heart was dilated. There were mitral valvulitis, left auricular endocarditis, acute fibrinous pericarditis, hepatitis, perisplenitis, and many Aschoff bodies and infarcts in the myocardium. The left circumflex coronary artery and main left coronary artery were thrombosed. There were gross lesions in the pulmonary artery.

Goldblatt has reported the case of a woman of thirty-eight years with a past history of polyarticular rheumatic fever, who died with heart failure and showed at autopsy deforming lesions (stenosis and regurgitation) of all four heart valves. The various valve orifices showed the following circumference measurements: mitral 7 cm., aortic 2.4 cm., tricuspid 8.0 cm., and the pulmonic 6.0 cm. (The normal valve measurements should be mitral 9 to 11 cm., aortic 7 to 8 cm., tricuspid 11 to 13 cm., and pulmonic 8 to 9 cm.)

Baehr and Schifrin have reported the rarity of diffuse glomerulonephritis in cases of rheumatic endocarditis; in 235 necropsied cases showing the latter condition, they found diffuse glomerulonephritis only three times (1.3 per cent). This is in striking contrast to its frequent occurrence following various diseases of proved streptococcal etiology, such as subacute bacterial endocarditis.

Cooley has reported careful blood culture studies in 25 cases of rheumatic fever and in ten nonrheumatic cases. All the cultures were negative except for a few late contaminations.

Jones and Jacobs have reported that treatment with a course of nirvanol (0.2 to 0.55 gram daily) produced no permanent benefit in three obstinate cases of chorea (all of them females) aged, twelve, nine, and seventeen years, respectively. One of the patients reacted dangerously. Tests were negative for any specific hypersensitiveness to the drug.

Master and Romanoff have reported a comparative clinical and electrocardiographic study of two groups of patients with rheumatic fever in the wards of the Mount Sinai Hospital in New York; one group of 33 cases received adequate salicylate therapy and the other group of 30 cases received no salicylate therapy and was used for control; the cases were taken alternately. "No essential difference was discovered. . . . The duration of hospital stay in the control group was forty-six days; in the salicylate group, forty-two days. One death occurred in each group. Polycyclic course, occurrence of pericarditis with or without effusion, and involvement of the lungs and other viscera were practically the same in the two groups. The electrocardiographic changes indicative of myocardial involvement revealed a surprising coincidence of changes in the two groups, qualitatively and quantitatively," estimated by the authors to exist in 100 per cent of both groups. The authors conclude that "there is no evidence that salicylates prevent cardiac complications or shorten the duration of hospital stay although they are at present the most efficient antipyretics and analgesics for the treatment of acute rheumatic fever."

Baehr, G., and Schifrin, A.: The Rarity of Glomerulonephritis in Rheumatic Fever and Its Significance. Libman Anniversary Volumes. P. 125, 1932.

Coburn, A. F., and Fauil, R. H.: Studies on the relationship of streptococcus hemolyticus to the rheumatic process. I. Observations on the ecology of hemolytic streptococcus in relation to the epidemiology of rheumatic fever. II. Observations on the biological character of streptococcus hemolyticus associated with rheumatic disease. III. Observations on the immunological responses of rheumatic subjects to hemolytic streptococcus. J. Exper. Med. 56:609, 633, and 651, 1932.

Cooley, L. E.: Blood cultures in rheumatic fever. J. Infect. Dis. 50:330, 1932.

Goldblatt, H.: Rheumatic Pancarditis with Functional and Anatomical Lesions of All Four Valves. Libman Anniversary Volumes. 2:507, 1932.

Jones, T. D., and Jacobs, J. L.: The treatment of obstinate chorea with nirvanol, with notes on its mode of action J. A. M. A. 99:18, 1932.

Master, A. M., and Romanoff, A.: Treatment of rheumatic fever patients with and without salicylates; a clinical and electrocardiographic study. J. A. M. A. 98:1978, 1932.

Schwarz, H.: An Unusual Case of Acute Rheumatic Fever in an Infant. Libman Anniversary Volumes. 2:1061, 1932.

(To be continued)

Case Records

ANTE MORTEM AND POST MORTEM

AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

AT THE

MASSACHUSETTS GENERAL HOSPITAL

Published under the direction of

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CABOT CASE RECORDS

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CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 19521

PRESENTATION OF CASE

DR. NEIL L. P. CRONE:* A Greek housewife of forty entered with a complaint of productive cough of two weeks' duration.

Present illness. Between two and three months before admission the patient had an attack of "grippe" characterized by cold in the head, sore throat and non-productive cough. She went to bed and remained there for two or three weeks. At the end of this period she felt considerably better and was able to leave the house, but developed a severe occipital headache, which had recurred at frequent intervals ever since. One month before entry she began to vomit all solid food eaten. The vomiting was accompanied by nausea and came on directly after meals. She had no pain, burning or other gastro-intestinal symptoms. During the interval she was taken to five physicians because of these headaches, and two weeks before entry at the advice of one of them had all her upper teeth removed under ether anesthesia. Twelve days before entry she began to develop a productive cough with bloody foul sputum which had steadily increased in degree up to the time of entry. She had lost twenty-five pounds in the past three weeks.

Family history negative.

Marital history. She had been married twenty-seven years. Six children were living and well.

Past history. Negative.

Physical examination. A moderately well developed and nourished woman sitting up in bed coughing frequently and raising foul blood streaked sputum. Breath foul. Head: directly over the midportion of the frontal bone was a subcutaneous nodular mass one centimeter in diameter. The eyes were negative. The upper teeth were entirely removed. The lower teeth showed moderate pyorrhea. The heart was normal in size. The sounds were regular and of good quality. There were no murmurs. The pulses were equal and synchronous. The radials were not palpable. The blood pressure was 130/90. Lungs: in the front of the right chest over the area from the second to the fourth ribs inconstant moist râles were heard and spoken and whispered voice were questionably increased. At the left base from the level of the angle of the scapula downward there was slight dullness with bronchial breathing, increased whispered voice, normal spoken voice and tactile fremitus. A question of amphoric breathing in this region was raised. The abdomen was negative. Pelvic examination showed cystocele and rectocele. The cervix showed bilateral laceration. It was roughened and red in appearance, oozing blood on slight pressure. (A period ceased the day before examination.)

Laboratory examination of the urine showed a specific gravity of 1.006 to 1.018 and a slight trace of albumin at one of eight examinations. The sediment showed many white cells and rare red cells in two specimens; no casts. Blood: hemoglobin 60 to 70 per cent, red cell count 2,900,000 to 3,600,000, white cell count 6,700 to 13,200. The differential count showed 85 polynuclears, 13 lymphocytes, 2 mononuclears, no eosinophiles, no basophiles. The red cells were not abnormal in size, shape or color. The sputum showed thin malodorous flecks of mucopurulent material. Spirochetes were found in small numbers on two of four examinations. Elastic tissue was present. There were numerous Gram-positive cocci in short chains. The stools showed a positive guaiac on one of two specimens. The Hinton was negative. Lumbar puncture on the sixth day showed an initial pressure of 320, left jugular compression 450, after 5 cubic centimeters 290, after 10 cubic centimeters 280, after 13 cubic centimeters 270; alcohol and ammonium sulphate negative; four cells; total protein 48, colloidal gold 0112332111, sugar 54, Wassermann negative.

X-ray. A chest film on the third day "shows dense mottled dullness involving the upper half of the right lung field. The dullness ends with a rather sharp border on its lower margin. The lower portion of the right lung and the entire left lung are clear. The heart and trachea are not displaced. There are no mediastinal masses. The appearance is that of a destructive process involving the right upper lobe. No cavities are demonstrable. Suggest reëxamination after postural drainage."

The physical findings were distinctly inconstant. On one occasion the visiting man was unable to find any signs in the patient's chest. Usually moist râles could be heard over the right upper lobe below the clavicle. In the same region spoken voice, whispered voice and tactile fremitus appeared to be increased. On one occasion definite dullness was present with bronchial breathing at the right apex.

A course of neoarsphenamin was started. On the eleventh day the signs at the right apex had entirely disappeared. An x-ray examination at this time showed evidence of clearing of the lesion at the apex but of extension downward to the lung. The sputum was distinctly less foul. On the sixteenth day dullness, distant bronchial breathing and increased tactile and

*Recently senior interne on the West Medical service.

vocal fremitus were noted for the first time at the right back beneath the scapula.

Apparent clinical improvement continued until the twenty-third day, when during a period of postural drainage the patient raised two mouthfuls of bright red blood. On the twenty-seventh day slight puffiness was noted beneath the eyes, and a slight trace of albumin appeared in the urine.

X-rays taken on the fourteenth day and again on the twentieth showed areas of decreased density which were characteristic of cavity formation. In successive plates the cavities appeared more definite and larger.

On the thirty-third day a marked personality change became evident. She gradually became lethargic and on one occasion fell out of bed. An x-ray film of the skull showed no positive evidence of increased intracranial pressure. A consultant found some choking of the left optic disk and made out an unsustained ankle clonus on the right. On the thirty-ninth day she was transferred to a surgical service.

DR. GEORGE W. HOLMES: I can add very little to what has already been presented, but I can show you the films.

This is an early film and shows dullness at the right apex with the abscess cavity and a tendency of the mediastinum to move towards the lesion.

Later films show some clearing of the apex, a gradual extension of the process into the lower lobes, and the appearance of bright spots with sharply defined lower borders characteristic of cavity.

The lateral view shows the lesions to be in the upper lobe.

In the last examination the cavities are larger, with definite fluid levels and possibly some further extension of the process in the lung.

DIFFERENTIAL DIAGNOSIS

DR. TRACY J. PUTNAM: Perhaps on looking back it is easier to connect the headache and vomiting with intracranial disease than it was when the patient first presented herself.

I think it is unfortunate that her teeth had to be sacrificed without further examination.

One other matter interests me in looking over the physical examination. When she was first admitted there was a subcutaneous nodular mass over the midportion of the frontal bone. I wish we might all have our fingers on that instead of reading about it; but apparently, now that we know the story as a whole, it did not have much to do with her intracranial condition. By this time it is quite obvious that it did not. I think the possibility of an epidural abscess and a "Pott's puffy tumor" over the epidural abscess might have been borne in mind.

I should like also to raise the point that long before her transfer to the Neurological Service her lumbar puncture showed increased intracranial pressure, increase in protein and a change in her colloidal gold curve. Oddly enough there is no increase in cells, but this it seems to me was enough to suggest intracranial pathology at that time. It is not at all suggestive of intracranial abscess. One even wonders if it were possible that she had some other intracranial condition in the first place and that the abscess was secondary to removing the teeth rather than the intracranial condition being secondary to the abscess.

The neurologic findings give us very little in the way of localization. It is no wonder that the intraventricular tap had to be undertaken to localize the lesion further.

As Dr. Mallory says, the presence of pulmonary suppuration and intracranial pathology almost invariably should suggest that the intracranial pathology is secondary to the pulmonary suppuration. It is a little puzzling to have the primary complaint that which could be explained perhaps on the basis of intracranial pressure.

FURTHER HISTORY

DR. CRONE: The pre-operative diagnosis was left frontal brain tumor, the postoperative diagnosis brain abscess in the right occipital lobe.

Under avertin anesthesia a transverse incision was made in the occiput. Drill holes were placed for a double ventricular tap, but on passing the needle through the right drill hole in the direction of the ventricle a large abscess containing much foul pus was encountered. It was not deemed advisable to continue the operation at this time on account of the patient's poor condition. A small pack was laid over the brain to permit it to adhere to the dura, which was left wide open and the scalp closed over it.

The day after operation the patient felt better, talking more readily and recognizing her friends. The improvement continued for two days; then her temperature started to rise. Her mental condition rapidly grew worse and on the forty-third day after admission she died.

CLINICAL DISCUSSION

DR. W. JASON MIXTER: This patient was in pretty desperate condition when it was deemed advisable to attempt localization of her intracranial lesion. I think we were all at sea as to the type of lesion, whether it was abscess or whether it was malignant disease, and whether her pulmonary suppuration was due to pulmonary malignant disease.

The finding of an abscess on attempting a ventricular tap was a great surprise to the surgeon. We had no idea of the localization of the abscess. There was no possibility of getting visual fields, which would be the one thing that might have told the story in this case. It seemed far wiser not to attempt to do anything further at that time than evacuate fluid from the abscess cavity and prepare for drainage at a subsequent date. Any attempt to drain the abscess at that time I think would have been fatal.

Clinical Diagnoses

Brain abscess.
Secondary meningitis.
Bronchiectasis.
Lung abscess, multiple.

Anatomic Diagnoses

Adenocarcinoma of bronchus with metastases to lungs, regional and retroperitoneal lymph nodes, kidneys and brain.
Pulmonary abscesses with metastatic brain abscess.
Cholelithiasis.
Cholesterosis.
Focal necrosis of adrenal.
Meckel's diverticulum.
Hydrothorax, right.
Endometrial polyp.

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy here was somewhat of a surprise. We found of course a lesion in the lung and a lesion in the brain, but the interesting part was that she had both cancer and abscess in the lung and both cancer and abscess in the brain. As far as one can go in attempting to put things together, I think she undoubtedly started out with primary cancer of the lung which was quite silent. Then she had a cerebral metastasis from that which was the cause of her first symptoms and for which she eventually had her teeth removed. Subsequent to the removal of her teeth she got a pulmonary abscess, and bacteria from that followed the malignant cells up to the brain, where one of the various tumor nodules had broken down completely and contained liquid pus.

We have had a considerable number of cases in which it has been quite impossible to make a differential diagnosis between primary cancer and abscess of the lung, and very often the cases do have both. The abscess usually lies beyond a point of occlusion of the bronchus by the carcinoma. I think this is the first case in which the secondary abscess has followed the primary cancer to the brain.

A Physician: Was the nodule on the sternum examined?

Dr. Mallory: The nodule was in the middle of the forehead and we did not feel justified in cutting into it. I think it might have been a metastatic carcinoma.

Dr. Crone: As I remember it, Dr. Mallory, she had had this nodule for years.

Dr. Mallory: That would make a difference. Have you any further comment, Dr. Putnam?

Dr. Putnam: I only want to emphasize the statement that when lesions are found in both the lung and the brain we have to suppose those in the lung are secondary to those in the brain. The reverse never occurs. I think I am right in saying that.

Dr. Mallory: I think a case of this sort is simply a trap for the diagnostician. The one thing that can be brought out is that cancer of the lung is almost always silent, abscess of the lung very rarely if ever.

CASE 19522

Presentation of Case

A single unoccupied Polish man of forty-two, formerly a rag worker, was brought to the Emergency Ward at six p.m., with acute abdominal pain and vomiting of fifteen hours' duration.

The patient was suddenly awakened at three o'clock on the morning of admission with sharp mid-abdominal pain. The pain was constant and severe enough to cause him to double up. Soon after the onset he began to vomit without relief of the pain. A physician was called who administered a hypodermic without relieving the pain. Shortly after the injection the patient began to shake but did not notice any sweating. The vomiting continued, the patient bringing up everything that he attempted to swallow, even water. The vomitus was dark brown; no blood was noticed. He had never had a similar attack. His bowels had not moved and he had passed no gas per rectum the preceding day.

Eight years before admission the patient had an attack of fever accompanied by swelling and pain in the joints of both feet. A diagnosis of rheumatic fever was made. Since that time he had noticed dyspnea on exertion, occasional attacks of palpitation and transient periods of swelling of the feet. For the past year he had had a persistent cough productive of small amounts of whitish sputum. There had been no hemoptysis. For the same period of time he had had occasional attacks of slight abdominal pain occurring at any time during the day without relation to meals, without loss of appetite, and unaccompanied by nausea or vomiting. During this past year he had lost fourteen pounds in weight.

Physical examination showed a well developed and fairly well nourished but obviously acutely sick man frequently retching and vomiting dark brown to nearly black rather foul liquid. The positive findings were as follows: He had severe pyorrhea. The heart was distinctly enlarged to the left, the apex impulse being seen and felt in the sixth space, two centimeters to the left of the midclavicular line. The heart was absolutely irregular, the rate 150. The sounds were of poor quality. There was a loud blowing systolic murmur heard best at the apex and transmitted to the left axilla. An early diastolic murmur was also heard at the apex. The radial pulse was irregular in force and rhythm, the rate averaging about 70 per minute. The blood pressure was 120/80. The lungs were negative except for a few râles at both bases. The abdomen was very rigid throughout, though deep pressure with considerable force elicited only moderate tenderness. There was no rebound tenderness. There was tympany throughout. No peristalsis was heard. Rectal examination was extremely painful high in the pelvis.

The temperature at entry was 98.6°, the pulse 75. The respirations were 32.

Laboratory examination showed a white cell count of 11,000. No urine could be obtained. No other examinations were attempted.

Operation was immediately performed. After it the patient ran a rapid downhill course, the temperature and respirations rising, the pulse and blood pressure falling. Vomiting continued. He died twenty-two hours after operation.

Differential Diagnosis

Dr. J. H. Means: The salient points in this case are that a man of forty-two, with what I take to be undoubted chronic rheumatic heart disease with aortic and mitral, possibly pericardial involvement, comes in with the picture of something very acute going on in his belly.

Since it may have a bearing on the acute attack, we may scrutinize the more chronic malady first. The attack of joint pain eight years before admission may or may not have been rheumatic fever. We have not enough information to prove this one way or the other. Since it was followed by heart disease we may guess that it was. Dyspnea on effort for some years with attacks of palpitation, edema of the feet and cough all suggest persistent low cardiac reserve. The physical findings of big heart, especially downward and to the left, with a mitral systolic and aortic diastolic murmur are characteristic of the double valve lesion of rheumatism. Indeed, I see no reason for considering any other etiology. The story is too long for syphilis, and fibrillation is almost unknown in syphilis, and he was undoubtedly fibrillating. There is no hypertension, and in its absence arteriosclerotic heart disease with so much hypertrophy would be distinctly unusual at his age.

My branding of the diastolic murmur as aortic needs some defense. If the observation that it is early is correct, it is almost certainly not mitral. It could be pulmonic, but its location is against that, also the probabilities. Aortic murmurs are heard not infrequently, only heard at the apex. I believe therefore that the murmur is aortic. The height of the diastolic pressure suggests that the degree of aortic regurgitation is not very great. I should like to know whether the peripheral signs of that lesion were present. The marked left ventricular hypertrophy with perhaps not a severe enough aortic lesion to account for it suggests the possibility of a chronic adhesive pericarditis. There is no evidence of gross congestive failure.

Now we come to the acute attack. The mid-abdominal pain was apparently very sudden and severe. It was accompanied by vomiting which did not give relief. The description of the vomitus leads one to believe that it was stercoraceous. If this is true, he must have had acute intestinal obstruction. This conceivably could have been due to any of the known causes of that condition, but if we wish to relate it causally to his heart disease I can see no way except on the basis of acute mesenteric infarction due to an embolus from his heart. Indeed, I feel quite sure that that is what he had. The white cell count is usually very high in mesenteric thrombosis; in this case it is not, but I do not believe we can discuss the diagnosis on that score. The findings in the abdomen I think fit better with infarction than anything else. With a type of obstruction that did not interfere with blood supply we might expect some hyperperistalsis above the point of stoppage. With a large embolus the whole bowel might be paralyzed by shock and a silent belly found, as here. The tenderness by rectum is compatible too, though not diagnostic of type.

From the suddenness of the onset I believe the obstruction high up in the small bowel. Obviously, immediate laparotomy was indicated.

Clinical Diagnoses

Rheumatic heart disease.
Mesenteric thrombosis.

Dr. J. H. Means' Diagnoses

Chronic rheumatic heart disease with aortic and mitral valves involved.
Probable chronic adhesive pericarditis.
Mural thrombosis of left auricle, whence an
Embolism infareting a portion of the small bowel high up and causing complete
Intestinal obstruction.

Anatomic Diagnoses

Rheumatic heart disease with mitral stenosis.
Mural thrombus, left auricle.
Embolism of branches of superior mesenteric artery.
Mesenteric thrombosis.
Pleuritis, chronic fibrous.

Pathologic Discussion

Dr. Tracy B. Mallory: The patient was explored five hours after entry and several loops of purplish red gangrenous ileum were found. There was no evidence of general peritonitis. The appendix and stomach were negative. The abdomen was closed and death occurred twenty-two hours later.

The postmortem examination confirmed the presence of gangrene in the third and fourth portions of the ileum. In the branches of the superior mesenteric artery supplying these loops a number of small slightly adherent emboli were demonstrated.

The heart weighed 400 grams. The mitral valve was moderately stenosed, measuring 5 centimeters in diameter. This longer leaflet showed marked calcification and the chordae tendineae were considerably thickened. A few fresh vegetations were present. There was a reddish brown adherent mural thrombus two centimeters in diameter on the wall of the left auricle. The other valves were all entirely negative.

The only other positive finding was an old fibrous pleuritis covering all surfaces of the lower lobe of the right lung.

A postmortem blood culture from the heart showed no growth.

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THE ONE HUNDRED AND FIFTIETH ANNIVERSARY OF THE FOUNDING OF THE NEW HAVEN COUNTY MEDICAL ASSOCIATION

A VERY interesting program has been arranged for the Sesquicentennial celebration of the founding of the New Haven County Medical Association, January 5, 1934.

This venerable medical association was formed when, in response to an invitation in the *Connecticut Journal*, "A group of physicians convened on January 5, 1784, at the Coffee House which stood on the site of the present Post Office, and the New Haven County Medical Association came into being." This was the ninth Medical Society to be organized in America and of this number only two others still exist, the Medical Society of New Jersey and the Massachusetts Medical Society.

The Massachusetts Medical Society was founded in 1781 and is the oldest Medical Society with a continuous existence in the United States. Although the New Jersey Society was founded fifteen years earlier, it suffered two intervening lapses of six and twelve years respectively, and therefore its continuous history dates from 1807. This brings the Massachusetts and the New Haven County medical organizations into close relation in the history of organized medicine in this country because, like the Massachusetts Society, the New Haven Association has complete and well-preserved records. Both are storehouses of valuable information.

The foundation of the New Haven Association is set forth as follows:

"We, the Medical Practitioners of the County of New Haven, convened in consequence of an invitation, in the *Connecticut Journal*, from the Faculty of the Town of New Haven, on this fifth day of January, 1784, having made choice of Colonel Leverett Hubbard, Chairman, and Doctor Samuel Darling, Secretary; do resolve ourselves into a Society to be called and known by the name of the Medical Society of New Haven County; plighting our Honor to each other for the strict observance of all such Regulations, as may be adopted by the majority of said society, formed for the following important purposes."

This preamble is supplemented by five declarations depicting the functions of this body.

This historical abstract abundantly shows the common interest in medicine exhibited by the New Haven County Association and the Massachusetts Medical Society, especially because the Connecticut State Medical Society, founded in 1792, was an outgrowth from the New Haven County Association, and the Connecticut and Massachusetts Societies have been associated with two great universities with important schools of Medicine. Medicine, in this country, is deeply indebted to Yale and Harvard.

The program of the Sesquicentennial exercises, arranged by the Committee of which Dr. George Blumer is Chairman, is as follows:

January 5, 1934
2:30 P.M.

Auditorium, Sterling Law Buildings.
Dr. Richard F. Rand, President, Presiding.

Addresses by Invited Guests:
Reverend Oscar E. Maurer.
Judge John L. Gilson.
President James R. Angell.

The Founding of the New Haven County Medical Association.
Dr. Creighton Barker.

The First Medical Transactions in America.
Dr. George Blumer.

The Founding of the Medical Institution of Yale College.
Dr. Harold S. Burr.

Events in the Association After 1840.
Dr. Thomas H. Russell.

4:30 P.M.

Reception.

New Haven Colony Historical Society, 114 Whitney Avenue.

Tea will be served.

8:30 P.M.

Auditorium, Sterling Law Buildings.

Convocation.

Address. Dr. Henry E. Sigerist
Director of the Institute of the History of Medicine, Johns Hopkins University.

9:00 A.M. to 6:00 P.M.

Exhibits.

Early Medical Manuscripts and Publications. Sterling Memorial Library.

Medical Memorabilia. New Haven Colony Historical Society.

Portraits of Physicians. Exhibition Hall, School of Fine Arts.

Supper may be obtained at the Yale Dining Hall from 6:30 to 8:00 P.M.

The Students' Common Room adjoining the auditorium in the Sterling Law Buildings will be open for members and guests preceding the evening convocation.

This important meeting warrants the expectation of attendance by the officers of the several State Medical Societies and especially representatives of the Massachusetts Medical Society.

SOME PROPOSED LEGISLATION

THE Massachusetts Board of Registration in Medicine has again introduced a bill which will, if enacted, give the Board some power of approval of medical schools from which it receives applicants for examination. The bill differs from that introduced last year in that it requires two years of college work before admission to a medical school; it requires that the candidate shall complete satisfactorily his medical course instead of spending four years of mere attendance; and it makes explicitly eligible the graduates of some high-grade foreign schools, the curricula of which, are not arranged in four years of thirty-two weeks each, but which, with five or six years of fewer weeks, may be considered equivalent to the approved course in the United States. It also makes explicitly eligible the candidates from schools in this country which have the four quarter system. The wording of the bill of last year would have permitted a degradation of the standards below their present level if the Board should see fit. The statutory requirement of two years of college work will prevent this in part, but it is not likely that the Board will ever seek to degrade the standards. The increased flexibility of the statutory provisions is a gain, and the new bill retains the important characterization of an eligible school as one "which is approved by the Board".

The phrase "some power of approval" which was used above is noteworthy. The new requirements are to apply only to candidates matriculating after the effective date of the proposed bill. Thus, all persons now eligible will remain eligible, and matriculants now in medical schools which now meet the requirements of the law will be exempt from the new requirements. Thus there is not the slightest suggestion of *ex post facto* law involved.

The question of policy on the part of the Board deserves attention. In view of the overwhelming rejection of the bill last year by the Committee on Public Health, 14 to 1, has the Board been wise in introducing a similar bill so soon, with the unchanged composition, and apparently unchanged complexion of the Legislature? Perhaps the complexion of the Legislature has changed, and the wisdom of the introduction can be determined better after than before the event. But the duty of the Board is to protect the public, and in its annual report to include "a statement of the condition of medicine and surgery in the Commonwealth". If in its opinion the public needs greater protection, the Board would be derelict in its duty to refrain from saying so, and from making recommendations to amend the situation.

The function of the Board with reference to proposed legislation is often misunderstood and last year there was some criticism because the Board did not "fight" for what it recommended. It is outside the province of the Board to "fight", to carry on propaganda for or against legislation. If it has special knowledge of any situation, it may lay information, with recommendations, before the Legislature at hearings, and in the usually belated Annual Report of the Board, it follows this procedure. If there is any "fighting" to be done, others but not the Board may participate.

It is to be hoped that this bill will receive even more attention from the public than the similar bill of last year, and from the Legislature, favorable consideration.

The recommendations of the Board with the draft of the bill to be considered by the Legislature appear on page 1367 of this issue.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

HOMANS, JOHN. M.D. Harvard University Medical School 1903. Assistant Professor of Surgery, Harvard Medical School. Surgeon to

Peter Bent Brigham Hospital. Address: 721 Huntington Avenue, Boston. Associated with him is

HASS, GEORGE M. M.D. Harvard University Medical School 1929. Instructor in Pathology at Harvard Medical School. Resident Pathologist, Peter Bent Brigham Hospital. Address: 721 Huntington Avenue, Boston. Their subject is "Regional Ileitis: A Clinical, Not a Pathological Entity." Page 1315.

JONAS, A. F. JR. M.D. Harvard University Medical School 1933. Surgical Interne, Johns Hopkins Hospital, Baltimore, Md. His subject is "An Evaluation of Signs and Symptoms in the Diagnosis of Extra-Uterine Pregnancy (Review of 90 Cases)." Page 1324. Address: Johns Hopkins Hospital, Baltimore, Md.

MORRISON, WILLIAM REID. M.D. Harvard University Medical School 1913. F.A.C.S. Associate Professor of Surgery, Boston University School of Medicine. Visiting Surgeon, Boston City Hospital. His subject is "Complete Surgical Removal of the Stomach for Hour-Glass Deformity Caused by Carcinoma." Page 1329. Address: 520 Commonwealth Avenue, Boston.

D'ERRICO, EMILIO. M.D. Tufts College Medical School 1923. Junior Visiting Surgeon for Gynecology and Obstetrics, Boston City Hospital. Associate Obstetrician, Lawrence Memorial Hospital, Medford. Assistant Junior Visiting Surgeon, Cambridge City Hospital. Instructor in Obstetrics, Boston University Medical School and Tufts College Medical School. His subject is "Spontaneous Intraperitoneal Hemorrhage of Unknown Origin Complicating Pregnancy." Page 1331. Address: 27 Bay State Road, Boston.

VERMOOTEN, VINCENT. B.A., M.D. Johns Hopkins University School of Medicine 1923. F.A.C.S. Instructor in Urology, Yale University School of Medicine 1928-1930. Assistant Professor of Urology, Yale University School of Medicine 1930-July, 1933. Address: New Haven Hospital, New Haven, Conn. Associated with him is

BERRY, REGINALD V. M.D. 1932. Their subject is "The Efficacy of Methenamine as a Bactericidal Agent in Urinary Tract Infections." Page 1332.

EDWARDS, EDWARD A. M.D. Tufts College Medical School 1928. Assistant in Surgery, Boston City Hospital. Instructor in Anatomy and Surgery, Tufts College Medical School. His subject is "The Status of Vasography." Page 1337. Address: 1571 Beacon Street, Brookline, Mass.

DRESSER, RICHARD. Ph.B., M.D. Johns Hopkins University School of Medicine 1921. Roentgenologist, Collis P. Huntington Memorial Hospital, Palmer Memorial Hospital, New England Deaconess Hospital, Boston, and Pondville Hospital at Norfolk. Consulting Roentgenologist, Worcester Memorial Hospital and Middlesex County Sanatorium. Visiting Roentgenologist Massachusetts General Hospital. Address: 695 Huntington Avenue, Boston. Associated with him is

SCHOLZ, FRANK. Technician, Collis P. Huntington Memorial Hospital, Boston. Address: 695 Huntington Avenue, Boston. Their subject is "A Device for Making Radiographs of the Gastro-Intestinal Tract." Page 1343.

WHITE, PAUL D. A.B., M.D. Harvard University Medical School 1911. Physician, Massachusetts General Hospital. Assistant Professor of Medicine, Harvard Medical School. His subject is "Cardiovascular Review for 1932." Page 1346. Address: Massachusetts General Hospital, Boston.

MASSACHUSETTS LEGISLATIVE NOTES

RECOMMENDATIONS OF THE BOARD OF REGISTRATION IN MEDICINE

1. In 1922, there was added to the requirements to be fulfilled by the applicant for examination for registration in medicine that of graduation from a high school; and also that the candidate be examined in physics, chemistry and biology. It is a fact that high schools do not, in general, give courses in these subjects which are adequate in the preparation for the study of medicine. Since the subjects are important they should not be eliminated but studied more thoroughly. This is in conformity with general custom, for all the other states require two years of college work in preparation for the study of medicine, and include physics, chemistry and biology either by explicit statutory enactment or by board ruling. Therefore, the Board recommends that two years of college work be required by Massachusetts before admission to the medical school.

2. Progress in the science and art of medicine makes greater demands in the educational preparation of the candidate for practice than were generally regarded as necessary forty years ago. In the year 1915, Massachusetts required that the candidate for examination should have received the degree of doctor of medicine or its equivalent from a legally chartered medical school empowered to confer degrees in medicine. It was supposed that such degree would represent the satisfactory completion of a course of medical instruction of not less than four years of thirty-six weeks each. The statute does not take cognizance of the travesty on medical education which exists in some schools which fulfill the statutory conditions. Therefore, the Board recommends that attendance upon a four-year course of medical instruction of

not less than thirty-two weeks in each year be supplemented by satisfactory completion of such course.

3. Some medical schools of high standing have a course of five or six years, with less than thirty-two weeks in each year. The statute should be more flexible in its provisions, so that graduates of these schools may become clearly eligible for examination. Therefore, the words, "or a course equivalent thereto" have been introduced.

4. The term "approved by the Board" is the wording most frequently found in the statutes of other jurisdictions, especially in the most recent legislation, and covers every contingency.

5. The exemption of students in actual attendance at the time of the passage of the bill in medical schools now eligible, is reasonable and just.

6. The exemption of physicians or graduates of schools which are now eligible, but which may become ineligible under the law, is reasonable and just. These candidates may have prepared for practice in Massachusetts under the present minimum requirements, and it may be impossible for them ever to fulfill the new requirements. It is the recommendation of the Board that the law as of the present time be permitted to apply to them.

THE COMMONWEALTH OF MASSACHUSETTS

In the Year One Thousand Nine Hundred and Thirty-Four

AN ACT relative to the Educational Qualifications of Applicants for Registration as Qualified Physicians.

Be it enacted by the Senate and House of Representatives in General Court assembled, and by the authority of the same as follows:

SECTION 1. Section two of chapter one hundred and twelve of the General Laws, as most recently amended by section one of chapter one hundred and seventy-one of the acts of nineteen hundred and thirty-three, is hereby further amended by striking out the second sentence and inserting in place thereof the following:—Each applicant who shall furnish the board with satisfactory proof that he is twenty-one or over and of good moral character, that he possesses the educational qualifications required for graduation from a public high school, that he has completed satisfactorily two years of college work before admission to the medical school, that he has attended and completed satisfactorily a four year course of medical instruction of not less than thirty-two school weeks in each year, or a course equivalent thereto, in one or more legally chartered medical schools and that he has received the degree of doctor of medicine, or its equivalent, from a legally chartered medical school having the power to confer degrees in medicine, which is approved by the board, shall, upon payment of twenty-five dollars, be examined, and, if found qualified by the board, be registered as a qualified physician and entitled to a certificate in testimony thereof, signed by the chairman and secretary.

SECTION 2. The additional qualifications herein required as a prerequisite to examination under said section two or corresponding provisions of earlier laws, shall apply only to persons matriculating in a medical school after the effective date of this act.

MISCELLANY

A RADIO MESSAGE PREPARED AND SPONSORED BY THE COMMITTEE ON PUBLIC EDUCATION OF THE MASSACHUSETTS MEDICAL SOCIETY FOR THE DEPARTMENT OF PUBLIC HEALTH

DANGER SIGNALS IN THE RHEUMATIC INFECTIONS OF CHILDHOOD*

BY ELI CHARLES ROMBERG, M.D.

Heart disease in childhood, and its chief cause, rheumatic fever in all its manifestations, constitute a tremendous health problem. Among school children in the United States heart disease is the fourth among the causes of death, and at least fifteen out of every one thousand school children have heart disease.

Since many of the cardiac deaths in adults are caused by heart disease contracted in childhood, the need of preventive work in the early years is clear. At present, there are many things about rheumatic infections that we do not know, but facts are gradually being accumulated and in time we hope to know as much of these infections as we do of other conditions.

It is impossible to discuss even superficially the problem of heart disease in children in such a short time as I have at my disposal. I am, therefore, only hoping to tell you of the importance of some of those conditions which serve as warnings of an impending rheumatic invasion, which may later lead to heart damage.

FAMILY HISTORY

Rheumatic infections tend to exist in some families. There is no doubt that rheumatic infections are frequently seen in more than one member of the family. Children born of parents with a past history of rheumatism should be watched more carefully. Fatigue, lack of appetite, transient pains in the extremities, palpitation, nosebleeds, and other familiar complaints would bear a great deal more weight in a child of such a family than in one with the negative family history.

Parents in the past have looked upon the pains which their children have complained of as growing pains, which they considered as normal manifestations of growth in childhood. Medically the term

*November 3, 1933. Station WBZ. 4:30 P.M.

"growing pains" refers to the fleeting joint and muscle pains of which children so frequently complain. They may be momentary in character and occur in any part of the body, particularly in the extremities, or they may persist for several hours. Sometimes the child complains of a knee or ankle so painful that he is unable to walk. Occasionally when arising in the morning the child finds his hand so stiff that he cannot open it. Other conditions sometimes cause a temporary discomfort in the joints particularly those occurring in connection with some acute infection. Bad posture and flat feet occasionally cause pains in the feet, ankles, and lower back. But the simple examination of the patient will inform us that this postural defect may be the cause of his discomfort. The danger lies in overlooking the more serious condition and putting it down as flat feet or postural defect. It is safer to assume in nearly all cases that all these transient pains are of rheumatic origin and to treat the patient accordingly. At least nothing will be lost in a wrong diagnosis. The fleeting pains, because they do not bring about any outward physical changes, are not looked upon as acute rheumatic fever. But frequent visits of such fleeting pains may do more heart damage than a case of real rheumatic fever showing red, hot, swollen, tender joints.

SKIN LESIONS

Various skin lesions may occur during an attack of rheumatic infection. There may be extensive mottling and flushing of the skin, or else discrete black and blue spots, varying in size, on areas which are not ordinarily exposed to bruises. These are evidences of hemorrhage under the skin which one associates with rheumatic infection.

NOSEBLEEDS

Nosebleeds, varying in intensity, and without any history of injury or undue violent effort, have frequently been observed in rheumatic patients. Particularly so does this occur as a warning before an acute rheumatic attack, or as an associated condition of a heart that is beginning to show damage for the first time, or comes as a warning that some rheumatic trouble is going to occur. Frequently nosebleeds may be the only outward manifestation of rheumatism, and may be the only fact of rheumatic interest in the history that may be uncovered after the discovery of heart damage. A patient with nosebleeds, with a complaint of progressive weakness, and with a history of rheumatism in some member of the family should be carefully and frequently observed.

The child whose heart is involved after rheumatic fever or St. Vitus' dance often remains anemic and does not gain weight. He may become undernourished. Rheumatic infections may even occur in children who are outwardly well developed and of normal weight and who appear healthy. Many mothers bring their children into the hospital because they are pale and thin and generally "run-down". This is the most common complaint in cases where we are first to discover heart disease. Their outward appearance and apparent loss of strength and their change in personality from one of healthy activity to one of apathy and disinterest appear as early symptoms. The appetite fails, the child becomes languid, pale, and changes in his behavior and his physical appearance may be observed.

Slight shortness of breath on exertion, such as going upstairs, or even getting up and about the room is one of the first symptoms. It is remarkable how much dyspnea or shortness of breath is borne by the child before he complains of it. He may be definitely panting after exercise, but will say he can breathe all right. Children have a great deal of grit. The child whose heart damage is slight at first, may go on for months before real shortness of breath is noted. Unfortunately many who should stop at this early warning frequently go on until their heart muscle is overtaxed and great damage takes place. The degree of this dyspnea or shortness of breath increases with the seriousness of the heart damage until we are called to see the patient with the completely broken down heart who has dyspnea even at rest.

A rheumatic manifestation very common in childhood in this climate is chorea, or what is commonly known as St. Vitus' dance. Many times this condition is overlooked because in its very early phases it simulates anything that might cause loss of appetite, pallor, irritability, and change of personality. It is only when children become restless and nervous and twitch a great deal that it is recognized by the more observant mothers. Even then a child is spanked or scolded for being nervous when he cannot help himself.

So far as we know chorea is due to some toxic or infectious agent which acts on the central nervous system by producing irregular involuntary contractions of the muscles, resulting in purposeless movements, and associated with muscle weakness and mental irritability.

Though chorea is a rheumatic manifestation it rarely occurs in more than one member of the family. It rarely, if ever, appears under three years of age and is most likely to occur in the highly strung, precocious child. The diagnosis can definitely be made, particularly when one has already learned a bit about the child's family history of rheumatism and his own recent behavior. The child's nervousness and inability to keep quiet rarely come at the beginning of the disease. There is a preliminary period of several weeks during which the child is pale, has a very poor appetite, does not care to play, and is content to sit about when previously he was full of life and energy. Deep circles appear under his eyes. The condition develops slowly and insidiously and the child becomes peevish, restless, irritable, and cries at the slightest provocation. Pretty soon one notes that he is awkward and cannot sit quietly

at school, is inattentive, fidgeting about in his chair. He begins to drop things and the teacher notices that he is writing poorly. He bites his fingernails and pulls at the buttons of his coat, shrugs his shoulders, twitches his lips and blinks his eyes. Associated with this there may be movements of some extremity particularly that which is the weakest and which is the one most involved. One, two, or all of the extremities may become involved and concentrated effort to do things exaggerates these symptoms. Frequently these symptoms may develop into a severe form particularly if a patient, who is potentially a choreic, is frightened or is exposed to some shock. The involvement is very extensive at the beginning of the disease and the motions are so violent that they interfere with speech or locomotion. Patients cannot feed or dress themselves. There may be such a loss of power in the extremity most involved that this part seems to be paralyzed.

All these conditions about which I have spoken are only some of the various ways in which rheumatism expresses itself in the human body. They simply are temporary conditions which cause discomfort to the patient limiting his activity for various lengths of time depending upon the severity of the involvement. We are interested in them particularly because they serve as warnings for the damage they may leave and in nearly sixty per cent of the cases the damage is related to the heart.

A great deal of preventive therapy can be achieved in rheumatic infections if we always keep in mind that rheumatic infections are very common in this climate, that they can occur from infancy and are difficult to recognize at that age. We must always remember the importance of a history of rheumatic infection in the family. Because of that fact, when a child presents suspicious symptoms, his heart, particularly, ought to be watched a little more frequently than a child with a negative family history, for after all it is the damage done to the heart that interests us. If we appreciate these insidious symptoms and give the child sufficient, prolonged bedrest, and other appropriate treatment, we may be saving the heart the damage that it would suffer if he tried to maintain the usual strain that a child puts to it in his active play.

"CANCER EXPERT" FOUND GUILTY OF FOOD AND DRUGS LAW VIOLATION

Lester Tilton, trading as Tilton Laboratories and Tilton Laboratories Research (Cancer) Treatment, Clinton, Iowa, after being found guilty by a jury in a United States Federal Court at Davenport, Iowa, was fined on November 27 the maximum penalty for a first offense under the Federal Food and Drugs Act, $200 on each of five counts, totaling $1,000, for selling preparations falsely and fraudulently recommended for the treatment of numerous diseases, according to Dr. P. W. Spickard, Medical Officer, Federal Food and Drug Administration. The attorney for the defendant has indicated his intention of appealing the case.

The drugs involved included "Pyroligeneous Compound No. 1," recommended for ulcers of the stomach, sore mouth, pyorrhea, sore throat, piles, and female troubles; "Pyroligeneous Compound No. 2" recommended for swollen glands, varicose veins, and goiter; and a "Healing Ointment," recommended for tonsillitis, sore throat, abscesses, appendicitis, pus conditions of pleura, and sore lungs. The Government successfully proved that all of the nostrums were falsely and fraudulently labeled, and thus were sold in violation of the pure food and drug law.

Analyses of the products showed that the ointment was a compound of petrolatum and turpentine, and that the liquids were small amounts of pyridine, ammonia, and ammonium compound. Tilton testified the liquids were fractional distillates of peat taken from his farm.

The Government introduced as witnesses several medical specialists who testified that each of the products was worthless for the purposes for which it was recommended and that no ingredient or combination of ingredients was efficacious in the treatment of all of the diseases for which each of the preparations was recommended. To further show the fraudulent intent of Tilton with respect to his claims for his medicines, other medical experts testified as to prior fraudulent acts of the defendant with respect to his claims for his cancer cure. The defendant, known as Dr. Tilton, accepted certain persons, sufferers from cancer, as patients who could be cured with his preparations. The medical experts who observed his treatment reached the conclusion that such treatment was an absolute fraud with the result that proper treatment for cancer was delayed.

Tilton, once a carpenter and later a locomotive fireman, manufactured the preparation at his home in Clinton, Iowa. — *Bulletin of U. S. Dept. of Agriculture.*

THE NAME OF VAN DYKE STREET CHANGED TO SHATTUCK STREET

As a tribute to Dr. Frederick C. Shattuck, long a teacher and friend of the Harvard Medical School, the name of Van Dyke Street, which adjoins the Medical School buildings, has been changed to Shattuck Street, it was announced December 21 by Dean David L. Edsall. As the street is a private thoroughfare, the change was made by authority of the Harvard Corporation and the neighboring hospitals.

Dr. Shattuck graduated from Harvard College in 1868, and the Harvard Medical School in 1873. From 1879 to 1912, he was a member of the teaching staff at the Harvard Medical School, serving as Jackson Professor of Clinical Medicine from 1888 to 1912. Following his retirement from active teaching, he was a member of the Board of Overseers from 1913 to 1919, and until his death in 1929 he remained actively interested in the progress and development of the Harvard Medical School.

FEDERAL EMERGENCY RELIEF

That provision for emergency relief which applies to illness and medical care is administered by an official in every city and town.

The *Boston Herald* of December 22, 1933, published a list of these officials.

Doctors and patients who wish to have the advantages of this measure must sign with the agent before the bills will be paid.

COMPARISON OF DISEASE INCIDENCE IN CONNECTICUT WITH 1932 AND SEVEN YEAR AVERAGE

MONTH ENDING DECEMBER 9, 1933

	1933					1932			
Diseases	Week ending Nov. 18	Week ending Nov. 25	Week ending Dec. 2	Week ending Dec. 9	Average cases reported for week corresponding to Dec. 9 for past seven years	Week ending Nov. 19	Week ending Nov 26	Week ending Dec. 3	Week ending Dec. 10
Botulism	—	—	1	—	—	—	—	—	—
Cerebrospinal Men.	2	—	2	—	—	2	1	—	—
Chicken Pox	110	141	106	162	111	113	58	103	124
Diphtheria	10	14	4	5	23	3	8	9	11
Dysentery Amebic	3	1	—	—	—	—	—	1	—
Encephalitis Epid.	—	1	—	—	—	1	—	—	—
German Measles	—	—	3	1	4	—	1	2	2
Influenza	3	17	4	10	4	29	10	18	7
Measles	5	13	10	10	51	11	6	13	23
Mumps	43	60	25	59	33	70	64	52	72
Pneumonia (Broncho)	53	57	48	69	22	40	18	50	32
Pneumonia (Lobar)	58	59	55	56	32	30	19	27	31
Poliomyelitis	—	—	1	1	1	—	—	—	—
Psittacosis	—	1	—	—	—	—	—	—	—
Scarlet Fever	60	71	54	76	55	55	64	73	90
Septic Sore Throat	—	1	—	—	2	—	2	—	1
Smallpox	—	—	—	—	2	—	—	—	—
Tetanus	1	—	1	—	—	—	—	—	—
Trichinosis	—	—	—	—	—	1	—	—	—
Tuberculosis (Pul.)	20	16	28	13	25	15	29	37	32
Tuberculosis (O. F.)	1	—	4	1	2	4	—	—	1
Typhoid Fever	1	1	—	—	4	1	1	—	1
Undulant Fever	2	1	—	1	—	—	2	—	1
Whooping Cough	54	52	31	44	69	75	66	84	109
Gonorrhea	19	36	36	56	36	34	22	37	23
Syphilis	32	25	67	48	51	30	55	75	45

Remarks: No cases of Asiatic cholera, glanders, plague, or yellow fever during the past seven years.

CORRESPONDENCE

THE PRE-ASEPTIC PERIOD

Editor, *New England Journal of Medicine*,

Five years before Dr. Worcester had his harrowing experiences in the Boston Lying-In Hospital, I was, one night, on my way to a narrow alley leading from North Street, Boston, to attend one of the two obstetrical cases needed before the Harvard Medical School would grant me a degree.

Fortified only by three or four didactic lectures given by Dr. William Richardson, and a small textbook on obstetrics in my side-pocket, I followed my guide through the streets. Reaching the house, I made an examination without antiseptics or even washing my hands. I learned absolutely nothing from this, and retired to a corner where under a lamp I read my book until a sudden cry from the bed announced that a new citizen of the North End had made his entrance into the world. I got a string somewhere, tied the cord, the placenta

came away, and my job was done. I was backed against a wall, forced to take a drink of whiskey, and then despite my protests, was escorted as far as Tremont Row by two ruffians armed with clubs to protect me (or so they said), from nocturnal marauders. One more such case, and I was supposed to be qualified to practice obstetrics.

A year later (an externe at the Boston City Hospital), I was detailed to give ether on operating day. A sponge and a bottle of ether were thrust into my hands, and I was told to get busy.

A gigantic fisherman with a hook embedded in his thumb lay on the table. A rather small attendant was at his side. Nobody else was visible. After a few whiffs, the patient seized the sponge, declared that he intended to murder me then and there, started up from the table, overpowered the attendant, and chased me into and across the operating room by this time well filled with students. Contrast this somewhat hectic adventure with the present everyday procedure.

When in due course I became surgical interne, it was my duty on operating day to take from a pincushion hanging on the wall, needles threaded with silk by an attendant with unwashed hands, to thrust these into the lapel of the coat reserved for operative work, stiff with pus and blood, if not with other more objectionable fluids, and then to draw through the buttonhole of said coat a number of silk ligatures, and, going to the sink to extract from a tub standing there a number of natural sponges, cleaning off as well as might be, the shreds of clotted blood from previous use. These were placed in an unsterilized tin basin, instruments were taken from the cases in the room, and after the carbolic spray had been started, and the operating surgeon had put on his own dirty frock coat, we were ready to operate. Arteries were ligated with the silk ligatures, one end cut short and the longer ends, bunched together, brought out at the lowest angle of the wound to provide drainage.

After a few days, gentle traction was made on them individually until, having cut through the vessels around which they had been tied, they were pulled away.

So common was secondary hemorrhage at about this time that a tourniquet was hung at the head of every bed that contained an amputation case, of which there were many, for severe compound fractures, for example, were so almost universally fatal that immediate amputation was often resorted to.

Time and again a frantic appeal from a night nurse caused me to leap from my bed, run at all speed to a ward and apply a tourniquet where it would do the most good, when and if the patient had not bled to death before I arrived.

There were no trained nurses, all temperatures were taken by the internes, all hypodermics given by them, suppuration was expected in all wounds, deaths from pyemia and septicemia too common to cause comment.

At one time, so frequently did hospital gangrene follow operations, that for some two weeks, as I remember it, only the most desperate cases were touched at all.

Three trained nurses from Bellevue finally appeared on the scene, and Miss Linda Richards opened a training school.

These nurses had a hard time, ostracized by the attendants, unappreciated by most of the visiting staff, and none too popular with the internes for whom they had the utmost scorn.

Nevertheless they soon began to improve conditions, introduced screens, and, wonder of wonders, came themselves into the male wards where no woman had up to that time permission to enter.

I speak of these things that it be not forgotten that the "world do move" and particularly as the last leaf upon the tree, for of all those associated with me in 1878-79, internes, visiting physicians and surgeons, nay so far as I know attendants, nurses and officials, I alone remain.

Sincerely yours,

S. B. Woodward, M.D.

SIR JAMES PURVES-STEWART EMPHASIZES HIS INTERPRETATIONS OF THE SOVIET RÉGIME

8 Buckingham Street,
Westminster, S. W. 1,
November 24, 1933.

Dear Mr. Editor,

Many thanks for the sheet from the *New England Journal of Medicine* of November 9th containing Mr. Kingsbury's letter, in which he criticises my little book "A Physician's Tour in Soviet Russia."

I hold no brief either for or against the Soviet régime. My observations on medical conditions in Soviet Russia simply state the facts as I found them. Perhaps Mr. Kingbury's political sympathies may have coloured his views. The facts as I have stated them are correct, that the medical practitioners in Russia are miserably paid, not only in comparison with other brain-workers, such as engineers, but even compared with some of the heavy manual-workers. The Soviet government is building beautiful new hospitals, sanatoria and baby-breeding farms, regardless of expense, but they economise severely on the salaries of their medical staff. Consequently the medical profession now offers no future for an ambitious man. He prefers to become an engineer, an aviator, or best of all a member of the Communist Party. I am truly sorry for these medical men who are gallantly struggling under conditions of economic stringency. True, they have only a 5-hour day, but most of them accept two billets in the day, so as to draw a double salary and even then they can just make ends meet.

I happen to have a personal friend in Russia, a pro-

fessor of international reputation. His name, for obvious reasons in his own interests, I must withhold. Before the War he had a good income. Out of his savings he bought himself a comfortable house in which to live with his daughter and son. Since the Revolution his house has been commandeered by the Government and he and his family are allowed to occupy two rooms. The remaining parts are divided up amongst various "comrades". Of course, the Communist will claim that all this is perfectly just and proper.

It seems to me that, boiling it down crudely to bedrock facts, everything depends on whether we accept the Communist dogma that all men are equal, and therefore deserving of equal rewards from the State, whether they are idle or industrious, extravagant or thrifty, intellectually dull or alert. Once the primary axiom is accepted, all the rest follows as a matter of course. But some of us cannot swallow the fundamental principle.

Believe me,

Yours faithfully,
J. PURVES-STEWART.

THE EXAMINATION OF SECONDARY SCHOOL STUDENTS

The Commonwealth of Massachusetts
Department of Public Health
State House, Boston

December 18, 1933.

Dr. William H. Robey,
President, Massachusetts Medical Society.

Dear Dr. Robey:

This Department would be very glad to have what help you, as President of the Massachusetts Medical Society, can give us.

Under the Re-Employment Program, it will probably be possible for us to employ some physicians for the purpose of examining secondary school students. We should be glad to hear from physicians, either men or women, who would be willing to give four or five hours a day to this work. The salary is to be at the rate of $5.00 an hour and transportation expenses are paid.

We hope to find physicians who are interested in preventive work and who enjoy contact with children. As part of the work will be in both the middle and the western part of the State, we hope, we should like to hear from physicians in Worcester County, in Connecticut Valley, and in Berkshire County, as well as from physicians in the region of Boston.

In order to obtain these positions, registration with this office is necessary. Blanks may be obtained upon application to the Division of Child Hygiene, State Department of Public Health, Room 546, State House, Boston, Mass.

Very truly yours,
FREDRIKA MOORE, M.D.,
Pediatrician.

RECENT DEATH

MORRISON—WILLIAM ALEXANDER MORRISON, M.D., of 80 Princeton Street, East Boston, died at the Boston City Hospital, December 19, 1933. He was the son of James and Jane (McKay) Morrison, and was born in East Boston in 1856. He was engaged in the drug business first in Boston, and later in Leadville, Colorado, where he served as sheriff for a time. After six years in the West he returned to Boston and entered the Harvard Medical School, from which he graduated in 1889.

He joined the Massachusetts Medical Society in 1887, and was a Fellow of the American Medical Association, a member of the East Boston Medical Society, the Boston Medical Library, the Harvard Club, and the Baalbec Masonic Lodge.

He is survived by his widow, Almira (Reid) Morrison, and three children, Jean E. Morrison, Dr. William Reid Morrison, and Dr. Gordon Mackay Morrison.

NOTICES

REMOVALS

DANIEL W. SHEA, M.D., announces the removal of his office to 1 Chestnut Street, Arlington.

HAROLD L. BABCOCK, M.D., announces the removal of his office to 99 Bay State Road, Boston.

RADIO HEALTH MESSAGES

DECEMBER, 1933

HEALTH MESSAGES

Sponsorship: Public Education Committee of the Massachusetts Medical Society and Massachusetts Department of Public Health.

Courtesy WBZ. Fridays, 4:30 P.M.

Dec.
29 **Preventive Medicine from Your Family Physician**

STATE HOUSE BROADCAST

Sponsored by the Massachusetts Department of Public Health.

Courtesy WEEI. Fridays, 1:15 P.M.

Health Subjects of Public Interest discussed by the Division Directors of the Department.

RADIO HEALTH FORUM

Queries from the public are answered under the sponsorship of the Department of Public Health.

Courtesy WEEI. Fridays, 5:00 P.M.

Questions on Health and Prevention of Disease may be sent to Radio Health Forum, State Department of Public Health, State House, Boston.

REPORTS OF MEETINGS

THE DUNHAM LECTURES

"Genetics and Pathology" was the subject of the Dunham Lectures this year. They were delivered in the amphitheater of Building C at the Harvard Medical School on the afternoons of November 20, 22, and 24 at five o'clock. The speaker, Dr. Otto Lous Mohr, Professor of Medicine at the Royal Frederiks University in Oslo, was introduced by Dr. Walter B. Cannon.

Professor Mohr opened the first lecture with a general discussion of the adaptation of organisms. He showed that normal adaptation may be disturbed by both external and internal factors. The latter are abnormalities of the germplasm or genotype. In some cases abnormality in the germinal constitution of an individual may not show its effect until there is a disturbance in the external condition.

Then followed a clear concise presentation of maturation processes in the germ cells which included a description of the human chromosome complex. In man there are forty-six autosomes and two sex chromosomes, XX in the female but XY in the male. All the chromosomes are in homologous pairs with the exception of the male sex chromosomes.

Next the speaker reviewed the history of the chromosome theory from the pioneer work of Mendel to that of Morgan and his associates. Mendel was pictured not as a secluded monk but as an active energetic personality whose one misfortune lay in being too advanced for his time. The Mendelian doctrines of unit characters, dominance, and segregation were well correlated with the recent work.

In regard to dominant genes, Dr. Mohr stated that, when heterozygous they usually produce characteristic disorders to mild degrees only. When homozygous, however, they may lead to profound disorders. The hereditary conditions of polydactyly, syndactyly, and platyphalangy were used in illustration.

Concerning recessive characters, it was explained that they do not appear in the phenotype unless in homozygous condition. Albinism, for example, is not manifested unless the individual is homozygous for the albino gene. The importance of consanguinity in the appearance of recessive characters thus becomes obvious. Consanguinity has been found in about one-fourth of the cases. Recessive genes as well as dominant genes may be affected in the expression of their potentialities by "modifying genes" which act to increase or decrease the manifestation of a given gene in the phenotype.

Sex-linked or crisscross inheritance were treated in detail both from the standpoint of the Drosophila experimentation as well as the human pedigree studies. One illustration used was that of color-blindness. This condition is transmitted from a color-blind father through his phrenotypically normal daughter to his grandsons. Females are not color-blind unless homozygous for the character. The same is true of hemophilia. There are no true female hemophiliacs, although recessive character is sometimes detected by a prolonged clotting time. The absence of true female "bleeders" is possibly due to intra-uterine death.

The phenomenon of non-disjunction was described and illustrated from the work of Bridges on Drosophila. Previous to this remarkable cytological demonstration the evidence for the chromosome theory of inheritance was only circumstantial. The closely related problem of gynandromorphism was also briefly touched upon.

Dr. Mohr ended by pointing out that, whereas a given gene may in some cases determine only one character, in other cases a single gene may determine a group of characters. In amaurotic family idiocy, for example, one gene determines the presence of idiocy, blindness, and muscular atrophy. Similarly, in craniocleidysostosis defective ossification of the cranium and absence of the clavicles are both produced by a single gene.

In his second lecture Professor Mohr elaborated upon his earlier statements concerning genes and their importance in transmitting traits from parent to offspring. He emphasized the fact that abnormalities need not necessarily be transmitted to the offspring in Mendelian ratios for there may be modifying genes to inhibit their expression. It is on this basis that some geneticists explain the discrepancies between theoretical and practical studies of hemophilia. Possibly a modifying gene is responsible for the rarity of this disease.

The speaker then went on to discuss at length the transmission of a number of hereditary diseases including Friedreich's ataxia, Huntington's chorea, and Wilson's disease. The importance of interpreting disease mechanisms in terms of genes was illustrated from the case of Swedish cattle. Most of the fine herds in that country are derived from two lines of sires. Each line possesses a gene transmitting an abnormality. If the pedigree of a given herd is unknown, knowledge of the hereditary mechanism allows a determination of the ancestry and numbers of defective offspring to be expected.

The final lecture of the series began with a discussion of intersexes. It was pointed out that each individual, whatever the sex, is endowed with both male and female determining genes. Hence, each sex possesses the potentialities of the opposite sex. The determination of sex does not depend on a single gene alone but on the sum total or balance of all the sex determining genes. If the balance is swung too far toward the male side, a supermale is produced; if too far toward the female side, a superfemale is produced. Intersexes appear when some influence reverses the balance

after development has begun. The degree of intersexuality depends on the extent of development at the time the change of balance occurred. Intersexuality was illustrated with the free martin reported by Lillie. The female of twin cattle under the influence of the hormones of its male twin develops external genitalia chiefly female while the gonad resembles a testis.

Human intersexuality is always in the female. No cases have ever been reported in the male. A number of women, when operated on for supposed femoral hernia have been found to possess a testis with spermatogonia and even spermatocytes. Virilism in the female, such as that caused by tumor of the adrenal cortex, is not true intersexuality; nor is hypospadias in the male. In the lower animals a number of cases of complete sex reversal have been reported, including that of Crew's hen which subsequently became a cock and actually fertilized eggs.

The speaker next directed his attention to the possible relationship between genes and hormones. According to Goldschmidt, genes are autocatalytic substances. Mutations arise when there are quantitative, rather than qualitative alterations, in these substances. By the injection of folliculin in the fowl Lillie has produced barring of the feather pattern, a character known to be determined by a gene.

The modification of genes was then described in some detail. That somatic changes do not affect the germplasm was shown by Castle in guinea-pig experiments. Pure albino animals, the ovaries of which had been grafted into them from pure black animals, became the mothers of black offspring only. Mutations produced by radiation, as first reported by Mulier, are usually recessive and lead to pathological states. This indicates the great danger in temporarily sterilizing a patient with x-ray. Careful analysis of the evidence on the effect of chemical agents, such as alcohol, on the germplasm reveals that no hereditable changes are produced.

Considerable evidence was presented indicating that heredity may be an important factor in tumor formation. Hereditary pigmented tumors occurring in Drosophila larvae and lethal in character have been reported. Heredity had been shown to be significant in xeroderma pigmentosum, neurofibromatosis, and certain other neoplasms. It is suggestive that carcinomas of the uterus, fundus, uteri, larynx and other organs have been found in identical twins although so far it has been impossible to establish a mechanism for the inheritance of cancer.

The great strides made in the knowledge of heredity were shown to have had widespread consequences. The concept of maternal impressions is rapidly disappearing. Acquired characters are no longer believed to have any direct effect on offspring. Intermarriage is now thought harmful only when undesirable recessive genes are present in a family. The hope has been raised that the human race might be improved by the application of eugenics but it has been found difficult to decide what characters are desirable. Sterilization has proved futile for race improvement because of the vast numbers that would have to be sterilized. It is indicated, however, not only to prevent the existence of undesirable offspring but even more to prevent the existence of undesirable parents. Prospective parents have become heredity-conscious and seek medical advice as to whether they should propagate. In persons with a heterozygous dominant, limited propagation may occasionally be justified but this does not include hemophiliacs.

In conclusion, Dr. Mohr emphasized the part the physician might play in the study of human heredity since he can best recognize pathological states. The employment of a trained geneticist in every medical center to study the material collected was urged.

MASSACHUSETTS PSYCHIATRIC SOCIETY

The meeting of the Massachusetts Psychiatric Society was held as scheduled on December 13 at 8 o'clock at the Boston Psychopathic Hospital. It was presided over by the President, Dr. Winfred Overholser.

The scientific program was furnished by the Research Staff of the Worcester State Hospital. The first paper, read by Dr. Freeman, entitled "The Arm to Carotid Circulation in Schizophrenia," was discussed by Dr. Samuel Gargill and Dr. Freeman. The second paper, "An Experimental Study of Hypnotically Induced Complexes," by P. E. Huston, D. Shakow, M. H. Erickson, was read by Dr. Huston and discussed by Dr. Ralph Kaufman, Dr. John C. Whitehorn, Dr. F. Lyman Wells, Dr. C. Macfie Campbell, the Vice President, and Dr. Huston.

In spite of the inclement weather there was a good attendance.

OSCAR J. RAEDER, M.D., *Secretary.*

NEW ENGLAND HEART ASSOCIATION

The New England Heart Association met on Monday, November 27, in the Amphitheatre of the Peter Bent Brigham Hospital, with Dr. Samuel Levine chairman.

The first speaker of the evening, Dr. Morton Brown, presented a paper on "Auricular Fibrillation in Non-Valvular Heart Disease." From a study of one hundred and nineteen autopsied cases, Dr. Brown concluded that most patients with auricular fibrillation without accompanying valvular disease show hypertension, with or without coronary artery involvement. Moreover, coronary artery disease was not in itself the significant factor in the development of auricular fibrillation. The most important in this regard was hypertension.

In a second paper, Dr. Richard Friedlander discussed auricular fibrillation in hearts without any other evidence of disease. This condition, Dr. Friedlander found, occurs more frequently than is generally recognized, and is occasionally diagnosed improperly as flutter or paroxysmal tachycardia. In the discussion following, Dr. Paul D. White pointed out that such cases should be regarded as functional disorders, like paroxysmal tachycardia or premature beats; moreover, that they are ideal for and quickly respond to quinidine therapy.

Dr. Samuel Levine presented the results of an analysis of the factors influencing length of life in angina pectoris. This interesting study was carried out by Drs. Levine and Eppinger. From a review of one hundred and forty-one fatal cases of established angina pectoris, it was ascertained that heredity is the most important etiologic factor in this disease. Thus angina patients with parents dying at the age of seventy or over lived five years longer than those with parents dying at sixty or under, a most striking prognostic point. Moreover, the female parent is more responsible for continuing vascular vulnerability than is the male. Such factors in angina pectoris as age of onset, hypotension vs. hypertension, angina at rest vs. angina with effort, previous tonsillectomy, cardiac failure, and obesity, have only little significant effect on the age at death or the duration of angina.

"The Results of Treatment of Angina Pectoris by Thyroidectomy" formed the thesis of the paper read by Dr. Eppinger. Of the thirteen cases invalided by the disease, seven obtained immediate and complete relief; five, moderate relief, in which there were occasional anginal attacks readily controlled by nitroglycerine. Dr. Elliott Cutler performed all operations. Four patients developed myxedema, the first signs of which appeared from thirty to thirty-eight days following operation. Two patients were given thyroid gland to relieve the myxedema, without any evidence of returning angina. In the discussion by Drs. Levine and Soma Weiss, it was brought out that the adrenalin test is a very dangerous procedure, and perhaps will be given up. It is not known whether thyroidectomy will prolong the lives of these patients. However, the procedure is still justified on the basis that some invalided patients can be given immediate and complete relief.

Dr. Levine emphasized that the rationale of thyroidectomy was not predictable on the basis of previous physiological work, and differed from Dr. Blumgart who claims that his work on the rate of blood flow formed the basis and logical background for thyroidectomy in heart disease. Levine pointed out that the low metabolism and the slow rate of blood flow that was found by Blumgart in myxedema would theoretically make one expect that producing an artificial myxedema by operation would leave the patient essentially unchanged, for not only would the demands on the heart be diminished by lowering the metabolism, but the supply would also be diminished by slowing the rate of blood flow. Furthermore, he stated that in angina pectoris there is no important slowing of the circulation to begin with, and therefore there should not have been any theoretical reason for diminishing the metabolism. Since the operations have been performed, other data have been discovered that help to explain the beneficial results of thyroidectomy, but as Dr. Levine made clear, the conception of this problem could not have rested on the previously known physiological work, as that is inadequate. He insisted that the practical experience with thyrocardiacs and the accidental removal of a normal gland which resulted in unexpected improvement made up the real background of this new work, and prompted him in the first instance to have this done at the Peter Bent Brigham and the Beth Israel Hospitals.

THE BOSTON PATHOLOGICAL SOCIETY

The second meeting of the Boston Pathological Society was held in the laboratories of the Department of Pathology of Boston University on November 15, 1933, with President Charles F. Branch in the chair.

The first part of the program consisted of demonstrations. Dr. Hazard of the Boston City Hospital presented a rare type of parathyroid tumor unaccompanied by bone changes. Dr. Tracy Mallory of the Massachusetts General Hospital demonstrated an example of interauricular defect in the heart and one of interventricular septal defect. In both cases the correct diagnosis, including the exact location of the congenital defect, was made by roentgenological examination. Dr. Shields Warren of the Deaconess Hospital presented three specimens: a lymphoblastoma of the mesentery of the small bowel, a spleen which contained large amounts of lipoid, probably cholesterol from a diabetic individual, and an unusual example of extremely malignant epidermoid carcinoma of the anus.

The second part of the program was given over to a paper on "Pulmonary Hypertension in Rats Living Under Compressed Air Conditions," by Dr. Granville A. Bennett and Dr. F. J. C. Smith. The authors presented the results of a series of studies upon the effects of compressed air upon albino rats exposed to an environment normal in all respects except for an elevation in barometric pressure to 3040 mm. Hg. (45 lbs. gauge pressure). Striking anatomical changes occur in the heart, lungs, and pulmonary arteries under this condition. These changes vary with the duration of exposure. After three days of exposure the lungs of adult rats show an acute reaction characterized by hyperemia, serous exudate in the pulmonary alveoli, marked perivascular edema, and pleural effusion. There is also a moderate inflammatory cell infiltration in the alveolar walls and perivascular spaces. This reaction is accompanied by thickening of the walls of the

small pulmonary arteries and narrowing of their lumina. All of these changes are most extensive on the fourth day of exposure when a small percentage of the adults die. Young rats under one month of age are relatively resistant to the toxic effects of increased oxygen tension and pathological examination of their lungs shows little more than perivascular edema. Both young and old rats become adapted to increased oxygen tension after one prolonged period of exposure so that on reëxposure they fail to develop these signs of acute oxygen poisoning.

After the first week of exposure the histological evidence of inflammation disappears and surviving rats develop progressive changes in the lungs which are characterized by a marked increase in the cellularity of the alveolar walls, patchy areas of atelectasis, and lesions in the small and large pulmonary arteries. The arterioles show progressive hyalinization and thickening of the walls, narrowing of the lumina, and the visible number is increased. These arteriolar lesions are very similar to those seen in the renal arterioles at autopsy in patients dying from progressive vascular nephritis with hypertension. The walls of the large pulmonary arteries double in thickness after ten days of exposure and become three to four times the normal thickness after one month. This thickening process is due chiefly to the new formation and condensation of fibrous tissue external to the media. The right ventricle and conus arteriosus are constantly dilated in rats dying of acute oxygen poisoning and in rats after prolonged exposure to compressed air. Small areas of scar tissue were found in the right ventricle of practically all rats after one month of exposure. In a few instances larger areas of scar tissue replacement which were visible on macroscopic examination were observed.

Direct measurements of the pulmonary arterial blood pressure after varying periods of exposure revealed that after 24 days the pressure readings were at the upper limit of the normal series and that after 31 and 38 days' exposure to compressed air, definite pulmonary hypertension existed in all rats.

The carotid arterial blood pressure of a small series of rats exposed to compressed air for thirty-eight days, decompressed and kept at normal barometric pressure for one week, was in each instance reduced to approximately one half normal.

In discussion Dr. F. J. C. Smith, co-author, defined toxic oxygen tension and stressed the fact that an increase in oxygen tension and an increase in barometric pressure were responsible for the early injurious effects noted in these experiments. He emphasized the observations that although some form of adaptation occurred during the first exposure so that acute oxygen poisoning did not reoccur on reëxposure the animals were living in a definitely injurious environment as was indicated by the continued loss of weight and by the changes which were described in the lungs. Dr. Smith pointed out that certain applications of these experimental studies could be made in caisson construction work in navy diving operations and in the use of oxygen in conditions of acute anoxemia.

The physiological aspects of oxygen poisoning were further discussed by Dr. Cecil Drinker. Dr. Behnke and Dr. Shaw elaborated on other aspects of oxygen poisoning and described psychic and neurologic aspects of the problem. Dr. Wolbach took issue with some of the implications and inferences which were made from these experimental studies in regard to the etiology of pulmonary hypertension.

SIDNEY FARBER, *Secretary.*

THE HARVARD MEDICAL SOCIETY

The Harvard Medical Society met in the amphitheater of the Peter Bent Brigham Hospital on Tuesday evening, November 28, at 8:15 P.M. Dr. S. B. Wolbach was chairman.

The meeting opened with the presentation of a surgical and a medical case. The former was that of a 42 year old woman, whose present admission was the third since June of this year. On her first entry she complained of a numbness and heaviness in the dorsum of her right foot. Diagnosis of thrombosis in the right anterior tibial artery was made; and the patient discharged.

One week later, weakness of the right arm and leg developed. This rapidly progressed to a complete hemiplegia. At the second entry, one month after the first, the patient had a hemiplegia and a choking of two diopters in the left disc. Mental reactions were slow. She was emotionally unstable, and speech was very thick at this time. Plain films of the skull and ventriculography confirmed the diagnosis of a very large tumor in the anterior portion of the left hemisphere. A left subtemporal decompression was done at this time, and the patient received four x-ray treatments with improvement. She was then discharged to Pondville. At this time she was incontinent. She then improved for two weeks, and then again slowly began to go downhill. One month after her second admission she reëntered for the third time. Right hemiplegia remained. The decompression was bulging. The patient was very slow mentally, and her vocabulary consisted of about seven monosyllabic words. Hemiplegia was of the spastic type, although reflexes were about equal on both sides. At operation, Dr. Zoilinger removed the entire left hemisphere, leaving only the basal ganglia on that side together with the choroid plexus. Four hours after the operation the patient was able to sit up and respond "all right". Her mental condition seemed much better. During the ensuing three days the patient could say, "all right," "drink," "sleep," "yes," and "thank you". Essential changes postoperatively were slight limitation of an already limited vocabulary, less ability to perform coördinated movements, decrease in rigidity of the paralyzed side, and a general decrease in excitabili-

ty of the reflexes. She continued to retain painful sensation, responding to pin-prick; also, upon moving the joints or compressing the muscles of the paralyzed side. The skin temperature reactions were normal; but the patient did not perspire. One week following operation the mental alertness began to subside, and she became more apathetic. The hemisphere removed weighed 740 grams.

In the discussion which followed the presentation of the case, the operative procedure was briefly considered. Dr. Cutler pointed out that, of the half-dozen cases reported in the literature, this was the first with such complete excision and the first in which the left hemisphere was removed. For this reason the observations on the speech of a right-handed patient were of particular neurological interest.

The medical case was presented next. A previous presentation had been made at the meeting on October 24. At that time a diagnosis of pulmonary moniliasis had been made. The sputa from this patient were negative for acid-fast bacilli but loaded with organisms of the monilia group. Urine and blood cultures were negative. X-ray examination showed consolidation of the right lower and middle lobes with some atelectasis. The apices and the entire left side were not involved. X-rays of the long bones showed areas of periostitis without bony involvement. The course of the case was gradually downward. The patient was made terminally comfortable by oxygen therapy. Ethyl iodide in large doses and intravenous arsphenamine had no beneficial effect. Death occurred one month after entry. Postmortem examination showed involvement of the lower and middle right lobes of the lung. Some miliary nodules were found in the liver. Cultures containing monilia were secured from the lung tissue. Histologically, the lesion was a squamous cell carcinoma, primary in the lung with metastases to the liver. Dr. Wolbach expressed the opinion that there is probably no such disease as primary pulmonary moniliasis.

The first of the two papers for the evening was presented by Dr. Shields Warren, pathologist to the Huntington and Palmer Memorial Hospitals. His subject was "Functioning Malignant Tumors of Ductless Glands." According to Dr. Warren, malignant tumors of organs such as the liver and intestine are commonly known to function. It has been observed that malignant cells in the intestine may secrete mucus, and in the liver, bile. In the ductless glands, however, functioning malignant tumors are quite rare. Of 250 cases of thyroid malignancy, only a "handful" have given evidence of functioning either in the primary lesion or in metastases.

A very striking and unique case, however, has been reported by Billroth. In this case complete thyroidectomy was performed to remove a tumor and, subsequently, myxedema developed. Later, with the growth of a metastatic lesion, the myxedema disappeared. Excision of the metastasis to relieve pain caused a return of the myxedema. The only other cases of functioning thyroid malignancy studied are those in which metastatic thyroid tissue showed colloid production histologically while extracts contained iodine and stimulated tadpole metamorphosis. The rareness of functioning thyroid malignancy fits in with the fact that malignancy is scarcely ever found in hyperthyroidism. In the parathyroid, not a single case of malignant functioning tumor has ever been reported.

In the pituitary, although functioning adenomata are relatively common, carcinomata are quite rare. Those which have been reported are associated with hypo- rather than hyperfunction of the pituitary. The same applies for the pineal gland.

The common pancreatic tumors are in the external secretory portion of the organ. Islet tumors are rare and, when functional, are almost always adenomata. Wilder reported a case in which a metastasis in the liver yielded an extract containing insulin or a similar substance. The liver in this case had an extremely high glycogen content of 8.25 per cent.

The adrenal glands show two types of malignant tumors, cortical and medullary. In the cortical carcinomata of youth, hyperactivity leads to precocious sexual development. Most of the cases of hyperactivity in adults occur in females and result in reversion to the male type. After operation, hirsutism disappears and female sex characteristics return but the male voice remains. Medullary tumors are characterized by paroxysmal hypertension, and only about ten per cent of these are malignant.

Tumors of the gonads are common. In the male they are usually non-functional. The most interesting are those in which there is development of a chorioepithelioma in a teratoma. These lead to gynecomastia, secretion of colostrum, and a positive Aschheim-Zondek test.

Functioning ovarian tumors are more common. These Dr. Warren classified in three groups. The first group includes the simple undifferentiated malignant tumors representing only the primordial germ cells and known as seminoma or dysgerminoma. Many patients with such tumors give evidence of pseudo-hermaphroditism. Some have shown true hermaphroditism. Following removal of the tumor, pseudo-hermaphroditism has persisted with one exception.

The second group consists of the arrhenoblastomas, the rarest of ovarian tumors. These have greater masculinizing power than have any of the others.

In the third group are the granulosal cell tumors, the commonest of the functioning tumors of the ovaries. They may occur at any age and always result in an accentuation of the secondary female sex characteristics. If the condition arises before

the menopause, menstruation is usually changed from normal to profuse. There is hyperplasia of the endometrium. If the tumor does not develop until after the menopause, its presence is often indicated by a resumption of menstruation.

In conclusion, Dr. Warren pointed out that functioning malignant tumors of the ovary, adrenal, cortex, and thyroid occur in that order of decreasing frequency. All others are merely pathological curiosities.

The second paper of the evening was presented by Dr. Charles C. Lund. His subject was "Multiple Primary Cancer, A Study of Cancer Susceptibility." Dr. Lund carefully distinguished multiple cancer from metastatic cancer. In the mouth, he pointed out, malignant lesions are frequently reoccurrences rather than recurrences. In about 1548 cases of buccal carcinoma 94 showed multiple cancer.

With the help of tables prepared by Dr. Wilson at the Harvard School of Public Health, Dr. Lund was able to show that for cancer the actual mortality was several times greater than that computed from expectancy figures. For deaths from all causes the actual and computed figures were nearly identical. Statistically, Dr. Lund demonstrated that a patient with cancer probably has a special tendency toward cancer and may die of that disease in spite of a cure of the original lesion. An obvious illustration is found in carcinoma of the buccal mucosa. Excision of a lesion is probably not curative because the irritating agent has affected the entire mucosa. It is therefore diseased whether or not it shows a characteristic leukoplakia, and repeated occurrence of cancer in it is quite probable.

Following the presentation of the paper, Dr. Wilson said a few words on statistical methods. He emphasized the need of more work to determine the relative importance of susceptibility and chronic irritation in the production of cancer.

Dr. Wolbach concluded the discussion by pointing out that one thing common to all irritating agents is that they maintain a continual reparative proliferation of cells antecedent to carcinoma of the epithelial type. He raised the question as to whether persons with increased susceptibility to cancer show a tendency to age more rapidly than normal.

COMPRESSION TREATMENT OF PULMONARY TUBERCULOSIS*

BY DONALD S. KING, M.D.

The compression treatment of pulmonary tuberculosis has changed the entire attitude toward this disease. At the present time, at the Rutland State Sanatorium, sixty-three per cent of all the patients are under some form of this treatment. At the Middlesex County Sanatorium, at the end of the year 1932, a little over forty per cent were being treated in this way. There are three important types of treatment: (1) artificial pneumothorax; (2) operations on the phrenic nerve; (3) thoracoplasty. The Jacobeus method of cutting adhesions through a thoracoscope is a very useful adjunct to pneumothorax treatment. Oleothorax, or the replacement of air by medicated oil, is helpful in certain cases which have developed fluid.

Compression treatment is effective because it gives added rest, obliterates tuberculous cavities, prevents the aspiration of tubercle bacilli into uninvolved portions of the lung, promotes lymph stasis and thus prevents toxemia, and stimulates the formation of fibrous tissue.

The technique of the different procedures is as follows: (1) Pneumothorax treatment requires frequent refills, usually with the maintenance of a negative pressure. The lung should be collapsed for at least a year after all symptoms have disappeared. (2) Phrenic nerve operation is performed through a small incision above the clavicle and consists either in crushing the nerve to give a temporary paralysis of the diaphragm, or resection of a few centimeters of the nerve (which is sometimes unsuccessful because the accessory phrenic is not cut), or the complete evulsion of the nerve. (3) Thoracoplasty has developed into a two-stage operation where sections of the ribs are removed close to the transverse processes with especial attention to removal of a section of the first rib. Recent observations have shown that to collapse apical cavities it is often necessary to remove practically all the first three ribs or to do an anterolateral operation in addition to the posterior resections.

Artificial pneumothorax is being used more and more in early cases. Its use is no longer confined to unilateral disease. Air given on one side often benefits the contralateral lung and there are many cases now under bilateral pneumothorax treatment. The phrenic nerve operation is useful largely as an adjunct to pneumothorax, thoracoplasty or some other treatment. Temporary paralysis of the diaphragm may be useful in early cases. Thoracoplasty is useful largely in unilateral fibrosing cases and at the present time is considered indicated in only about five per cent of the sanatorium cases.

Fluid is often a troublesome complication of pneumothorax treatment and tuberculous empyema, which sometimes develops, is of very serious import. Operative shock, postoperative pneumonia, spread of the tuberculous process to the contralateral lung, and secondary wound infection are occasional complications of thoracoplasty.

The good results of artificial pneumothorax are without doubt established. There is still some question as to the ultimate value of the phrenic nerve operation as a primary form of treatment. Thoracoplasty is of undoubted benefit in properly selected cases, though the closure of large apical

*A digest of an article presented before the South End Medical Club, November 21, 1933.

cavities requires extensive resection of the upper ribs. Many of the failures in the past have been due to a lack of this form of rib resection.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

December 27-30—American Association for the Advancement of Science, Section N (Medical). See page 1251, issue of December 14, also page 1313, issue of December 21.

January 4—Faulkner Hospital Clinical Meeting will be held at 5:00 P.M.

January 15, 1934—Boston Medical History Club. Speaker: Professor Henry E. Sigerist, Director of the Institute of Medical History of Johns Hopkins University.

JAMES F. BALLARD, Secretary.
Boston Medical Library, 8 The Fenway, Boston.

January 15, 16, and 17, 1934—American Conference on Birth Control will be held at the Mayflower Hotel, Washington, D. C.

February 16 and 17, 1934—The New England Hospital Association is holding its Twelfth Annual Meeting at the University Club, Boston. For details write Dr. A. G. Engelbach, Massachusetts General Hospital, Boston.

April 16-20, 1934—The American College of Physicians will hold its Eighteenth Annual Clinical Session in Chicago at the Palmer House. For information write Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

July 24-31, 1934—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schnlz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 4, 5, 6, 1934—International Union Against Tuberculosis will be held in Warsaw. For particulars address The National Tuberculosis Association, 450 Seventh Avenue, New York, N. Y.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH DISTRICT MEDICAL SOCIETY

January 3—The Ninety-Third Semi-Annual Meeting will be held at the Elks Club Rathskeller, Summer Street, Haverhill, at 12:30 P.M.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

Wednesday, January 3—Danvers State Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Clarence A. Bonner, Superintendent of Danvers State Hospital. Subject: Recent Experiences in Foreign Clinics.

February 7—Council Meeting, Boston.

Wednesday, March 7—Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Frank H. Lahey, Boston. Subject to be announced. Film Electrocardiogram.

Wednesday, April 4—Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speakers: Dr. Elliott P. Joslin and Dr. Howard F. Root, Boston. Subject: "Tuberculosis Complicating Diabetes."

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.
221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings will be held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings will take place on January 10 at Melrose, March (2nd Wednesday) at Wakefield, and May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.
76 Church Street, Winchester, Mass.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

Meetings will be held on January 31, and April 25 (Annual Meeting).

T. A. STAMAS, M.D., Secretary.
226 Central Street, Lowell, Mass.

NORFOLK DISTRICT MEDICAL SOCIETY

Postgraduate Course. See page 1184, issue of December 7.

January 28—Tentatively Roxbury Masonic Temple, 8 P.M. Continuance of Symposium on Diseases of the Blood. Dr. Dameshek and Dr. Straus.

February 27—Place, time, subject, and speaker to be announced.

March 27—Place and time to be announced. Dr. Edward A. Edwards and Dr. Henry H. Faxon. Symposium on the Treatment of Varicose Veins.

May—Annual Meeting. Place, time and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.
1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

January 4—12 noon at Norfolk County Hospital. Speaker to be announced.

February 1—12 noon at Norfolk County Hospital. Stated Meeting. Speaker: Dr. Sara Jordan. Subject: Stomach Ulcers.

March 1—12 noon at Quincy City Hospital. Program by the hospital staff.

April 5—12 noon at Norfolk County Hospital. Speaker: Dr. Elliott P. Joslin. Subject: Diabetes.

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.
Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

January 31—General Meeting in association with the Boston Medical Library and the Trudeau Society. Speaker: Dr. Lawrason Brown of Saranac Lake.

March 22—Clinical Meeting at the Massachusetts Memorial Hospitals.

April 25—Annual Meeting at the Boston Medical Library. Election of Officers. Scientific Program, titles and speakers to be announced.

The Medical Profession is cordially invited to attend all of these meetings.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary,
311 Beacon Street, Boston, Mass.
ALEXANDER S. BEGG, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

All meetings to be held on Wednesdays as follows:

January 10—Dinner and scientific program at the Worcester City Hospital, Worcester, Mass.

February 14—Dinner and scientific program at the Worcester State Hospital, Worcester, Mass.

March 14—Dinner and scientific program at the Memorial Hospital, Worcester, Mass.

April 11—Open date.

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester, Mass.

BOOK REVIEWS

Fractures. By PAUL B. MAGNUSON. Published by J. B. Lippincott Company. 466 Pages. Price $5.00.

In latter years fractures and dislocations have provided a fertile field for literary cultivation. There now exist so many good books dealing with the subject that when the surgeon learns of the appearance of another new book, his first reaction is apt to be one of irritation. It was somewhat in this mood that the reviewer examined Magnuson's book. He knew of the author's reputation and experience in the treatment of fractures, but he felt that the book must possess unusual qualities to justify itself. He noted approvingly its smaller size in comparison with the ordinary textbook, and the sales price, half that of the usual. He noted the excellent illustrations which are ample for the purpose and yet not burdensome. He read the preface which

stated that the book was written primarily for the benefit of the man who first treats the fracture. Beginning to glance through the text, he quickly became interested, and ended by reading practically from cover to cover.

The style is simple and readable, the subject is clearly and thoroughly presented, the principles taught are sound, and emphasis is continually placed upon the anatomic facts which must be taken into account in dealing with each type of lesion. It is not a compendium, nor does it attempt to be encyclopedic. It is an exposition of the system of treatment developed by a surgeon who is an individualist, but has had a large experience and is endowed with good judgment and mechanical sense. He employs traction in all closed reductions, and secures it to good mechanical advantage by the ingenious use of a bandage placed about the operator's shoulders, which leaves the hands free to manipulate the fragments. He finds even the difficult, comminuted fractures of the humeral condyles generally solvable by continuous traction and countertraction properly arranged, and believes closed methods preferable here. He points out the causes of unsatisfactory results and emphasizes the dangers. In fractures of the femoral shaft he uses adhesive or skeletal traction in conjunction with the Thomas splint. One may not agree with all the operative methods described, the use of silk or wire where fascia lata might be substituted with advantage, but he at least describes a method for dealing with the lesion which may be readily modified by any surgeon with other ideas. There is a certain unevenness about operative details which should be remedied. Thus a description of the operative management of fractures of both bones of the forearm is deliberately omitted on the ground that the operation, while frequently necessary, is too difficult for any but the most experienced surgeons, yet the author describes in detail his operation for old ununited fractures of the hip, which presumably would require even more skilful operative ability.

We would criticize an apparently too slavish devotion to the position of abduction in treating fractures of the neck of the humerus when it has been shown that many of the comminuted fractures in this region do well when treated by early mobilization with the arm by the side; the advice to excise dislocated semilunar bones of the wrist without ever attempting replacement; the conclusion based upon what we consider insufficient personal evidence that fractures of the carpal scaphoid give better results when treated by massage and mobilization instead of by splinting; and the lack of a suitable classification of the different types of ankle fractures. The author leaves us in doubt as to the best treatment of fractures of the neck of the femur, stating that satisfactory results are obtained in only fifty per cent of the cases following Whitman's method of treatment, and inferring that better results can be obtained by operative treatment, but no description is given of the preferred procedure. Does the author achieve the object for which he writes, namely, that of instructing the man who first sees the fracture? In the main, yes; in certain details, no; on the whole better than most authors.

But let not this criticism deceive. It is a splendid book, stimulating and well worth while for even the most experienced surgeon. We welcome this newcomer to the shelves of fracture books, and wish for it many and better editions.

The Therapeutic Agents of the Quinoline Group. Cinchophen, Plasmoquine, Nupercaine, Quinine and Acridine Dyes. The Relation between their Chemical Constitution and Pharmacologic Action. By W. F. VON OETTINGEN, M.D., Ph.D. Published by The Chemical Catalog Co., Inc., N. Y., June 27, 1933. Price: $6.00.

This book is one of the monograph series of the American Chemical Society. The general plan of the series is to provide summaries of important topics in chemistry, in such a form as to be available to other workers in allied fields. Obviously, this indicates that the plan of the book shall be a brief discussion of the chemistry of the quinoline derivatives followed by a review of the pharmacologic effects of those that have been studied, with a brief discussion of the relationship between the two. This plan has been followed in this monograph after each section.

The book is divided into twelve chapters, each of which is concerned with a single group of quinoline derivatives. Of course this group contains many products of clinical interest. Among the hydroxyl derivatives are "quinosol" and "yatren". The quinoline carboxylic acids, of which cinchophen and "nupercaine" are both examples, are given a chapter. Similarly, "plasmoquine" is considered in the aminoquinoline group. The review of the quinine group itself is of great thoroughness and of great value. The discussion of the action of quinine and quinidine on the circulation is worth the reading of every cardiologist. Among other important compounds, "acriflavine" is also discussed. Not least valuable are tables showing the comparative effects of various derivatives. One particularly valuable table is a complete list of the reported fatalities after the administration of cinchophen and another showing the severe intoxications with recovery. An extensive study of the anti-malarial effects and other effects of the quinine derivatives is also given.

At times, as is inevitable in a review which is as compressed as this one, some of the sentences lack clarity, and the comments are necessarily brief although the bibliography provides the reader with the means of investigating further. The book is written in rather reportorial style without critical comments on the work by the author, although both sides are presented when conflicting evidence exists in the literature.

The book represents an extraordinarily valuable

contribution to the reference literature and should be readily available in all hospitals and libraries and to any workers who are using any of the many drugs that have been developed about the quinoline nucleus.

Annual Report of Surgeons General, U. S. Navy, 1932.

This annual report of 198 pages is rather difficult to review except in part, being filled with long tables of financial and medical statistics. There are, though, some matters of interest to the practicing physician. An example follows:

On page 73 is an interesting discussion of appendicitis. The increased incidence of acute appendicitis that has been noted in the civil population also occurred in the navy. The comparative figures do not go back beyond 1928, but then the rate of admission for this disease was 728 per 100,000 while in 1931 it was 927. This represented in 1932, 1,045 such admissions. Appendectomy without drainage was performed in 894 cases with one death and with drainage in 28 cases with six deaths. There were also three other deaths, presumably in cases not operated on. Appendectomy was also performed 430 times with the diagnosis of chronic appendicitis with no deaths. In spite of the fact that the patients in this series were probably in much better general physical condition than corresponding patients in civil life, this seems to be an extraordinarily good record when one considers the fact that many of these cases must have arisen under conditions when early and proper operative treatment were either difficult or impossible to secure. It makes the reviewer wonder whether many great civil hospitals with splendid facilities and large staffs cannot possibly learn something by a study of the methods of the Navy in its handling of this problem.

Some Modern Extensions of Beaumont's Studies on Alexis St. Martin. By W. B. CANNON. Beaumont Foundation Lectures. Reprinted from *The Journal of the Michigan State Medical Society*, March-May, 1933. 87 Pages.

The one hundredth anniversary of the publication of William Beaumont's famous book on "Experiments and Observations on the Gastric Juice and the Physiology of Digestion" has led to a brilliant series of papers on both the author and the subject. The book itself, long since a very rare item and only to be found in the hands of a few collectors, was republished, fortunately, in 1929 by the Harvard University Press, at the time of the Thirteenth International Physiological Congress in Boston. In the October 1933 issue of the *Yale Journal of Biology and Medicine* there appears an excellent sketch of Beaumont by Dr. Walter R. Steiner and a bibliographical description of the editions of Beaumont's book, with some letters of Beaumont's by Charlotte H. Peters and John F. Fulton. One letter especially, from Beaumont to a bookseller in New Haven, throws new light upon the early distribution of his important publication. In addition, as the result of the William Beaumont celebration, October 5, 1933, at the New York Academy of Medicine, there has been published in the *Bulletin* of this organization a series of papers, including one by Harris A. Houghton on the contract that Beaumont made with Alexis St. Martin, in which this remarkable Army surgeon guaranteed to pay St. Martin one hundred and fifty dollars for a year's service and found.

The small volume by Dr. Cannon is a reprint from the *Journal of the Michigan State Medical Society* of the Beaumont Foundation Lectures for 1933. The author, using Beaumont's book as a basis for his dissertation, considers, in separate chapters, such subjects as "Thirst and Hunger," "Digestion and Health," and "Disturbances Produced by Pain and Emotional Excitement." He thus brings into brief review all of the important work on these subjects accomplished by physiologists in the last one hundred years.

The book is brilliantly written, but, unfortunately, is poorly produced, on inferior paper, with a cheap cover. Such an important contribution as this deserves a better dress.

Manuel D'Expertise en Otologie. By ANDRÉ MOULONGUET. Published by Masson et Cie. 108 Pages. Price 16 fr.

This manual of 103 pages is very valuable for aurists engaged in insurance, military or compensation work.

The author reviews the various tests for unmasking malingerers; the types of cases encountered in industrial accidents and cases arising in military life and in addition the methods employed in dealing with them. He also considers the degree of risk involved in awarding life insurance to people with diseases of the ears.

BOOKS RECEIVED FOR REVIEW

An American Story of Precipitated Chalk by T. G. Leek. Published by Industrial Chemical Sales Company, Inc. 25 Pages.

Physiological Health edited by Jay B. Nash. Published by A. S. Barnes and Company. 308 Pages. Price $2.00.

The Health and Turnover of Missionaries by William G. Lennox. Published by The Advisory Committee of the Foreign Missions Conference, New York. 217 Pages.

Metabolic Diseases and Their Treatment by Dr. Erich Grafe. Published by Lea & Febiger. 551 Pages. Price $6.50.

Medical Art Calendar for 1934. Published by J. Philip Kruseman, 'S-Gravenhage. Price $1.50.